VOLUME 16 NUMBER 5

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ARCHIVES OF SURGERY

VOLUME 16 MAY, 1928 NUMBER 5

LATE TREATMENT OF BURNS

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AND
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NEW YORK

In a previous communication we discussed the immediate treatment for cutaneous burns. We concluded that treatment with tannic acid excelled other known methods, for the following reasons: (1) It diminishes pain; (2) it prevents fluid depletion; (3) it decreases toxemia, and (4) in first and second degree burns, it allows epithelization to proceed while the membrane is in place.

This splinting of the granulation tissue by the rigid tannic acid membrane while epithelization is in progress seems to prevent contractions of the scar tissue (figs. 1, 2 and 3).

During the past two years, we have had the opportunity to treat several patients with severe burns, and we have learned some aids in late treatment which may be of value. We wish to review briefly the early treatment of burns by tannic acid, and then to discuss the following factors that occur after the primary treatment: (1) infection beneath the tanned membrane; (2) treatment of the granulating surfaces, and (3) the causes of failure in attempts to graft skin on the granulating surfaces.

One hundred and fourteen patients with burns were treated with tannic acid at the Lincoln Hospital from Jan. 1, 1926, to Sept. 1, 1927. Twenty-three died, a total mortality of approximately 20 per cent. The cause of death as analyzed depended on the age of the patient, the extent of the body area involved and the complications which may have arisen. The ages varied from 9 months to 61 years. The length of hospitalization varied from two hours to seventy days. We have attributed the deaths occurring within forty-eight hours to shock. The deaths occurring after this period we have classified as deaths due to infection and toxemia. Among the complications in this group were parturition, two cases; poisoning from illuminating gas (condition present on admission), chronic pulmonary tuberculosis, acute nephritis, fracture of the skull and mandible, and fracture of the pelvis with multiple lacerated wounds of the scalp, one case each. In this series, eleven patients died of shock, or approximately 10 per cent, and twelve died of toxemia and sepsis, a mortality of approximately 10.4 per cent.

In reviewing our previous series, we found that deaths from burns of similar extent and severity for which treatment by picric acid and dry air was being given, were approximately 40 per cent, and deaths due to debridement resulted in a mortality of 57 per cent. These figures show a definite decrease in mortality attributable to treatment by tannic acid.

The table gives the mortality in cases of burns.

IMMEDIATE TREATMENT FOR BURNS

On arrival at the hospital, the patient is treated for the immediate shock. Morphine is administered, and either a hypodermoclysis or a transfusion is given as soon as possible. The skin is cleansed as far as can be done without creating any greater shock. The skin covering the blisters is removed, and dressings saturated with a 5 per cent aqueous

Mortality Rates in 114 Cases of Burns

Decades	1	2	3	4	5	6	7	Total
Deaths occurring in 1-48 hours (shock)	5	2	..	2†	1	0	1	11
Deaths from toxemia and infection	3	2	2	3	..	..	..	10
Deaths probably attributable to other causes	..	..	1‡	..	1§	..	..	2
Number of cases	8	4	3	5	2	0	1	
Percentage	34*	17	13	21	8	0	4	
Deaths	..	..	..	..	..	..	..	23
Percentage mortality	..	..	..	..	..	..	..	20.1
Percentage mortality due to shock	..	..	..	..	..	..	..	10
Percentage mortality due to toxemia and infection	..	..	..	..	..	..	..	10.1

* Note the high mortality in the first decade.
† Patient also had fractured skull (1 case).
‡ Lobar pneumonia and suppurative pleurisy.
§ Lobar pneumonia and acute nephritis.

solution of tannic acid are applied. These dressings are applied loosely and kept saturated with the solution for twenty-four hours or until the burned area is tanned a mahogany brown. Other authorities have advised using a spray of tannic acid, without the application of dressings. We have preferred the loose application of gauze saturated with tannic acid. No bandages or constricting apparatus are applied. When the burned area is sufficiently tanned, all dressings are removed, and a tent is made to prevent pressure of the bed-clothes. Warm air is created by inserting electric lights. Care should be taken to keep sterile pads or sheets beneath the burned areas that rest on the bed. Infection can, and frequently does, occur beneath the tanned area (fig. 4). Every effort should be made to prevent its inception.

We have found that patients with burns need constant care, and badly burned patients should have a special nurse. The burnt areas must be kept scrupulously clean, and the patient's position must be constantly changed. Forcing the fluids is important, as it diminishes the

Fig. 1.—Low powered view of the skin and subcutaneous tissue in a child, aged 8, who was treated by tannic acid. The sections were removed four days after the burn. *a* indicates the tannic acid membrane; *b*, the separation zone; *c*, the hair follicle and *d*, the subcutaneous connective tissue. (From Ann. Surg., July, 1926.)

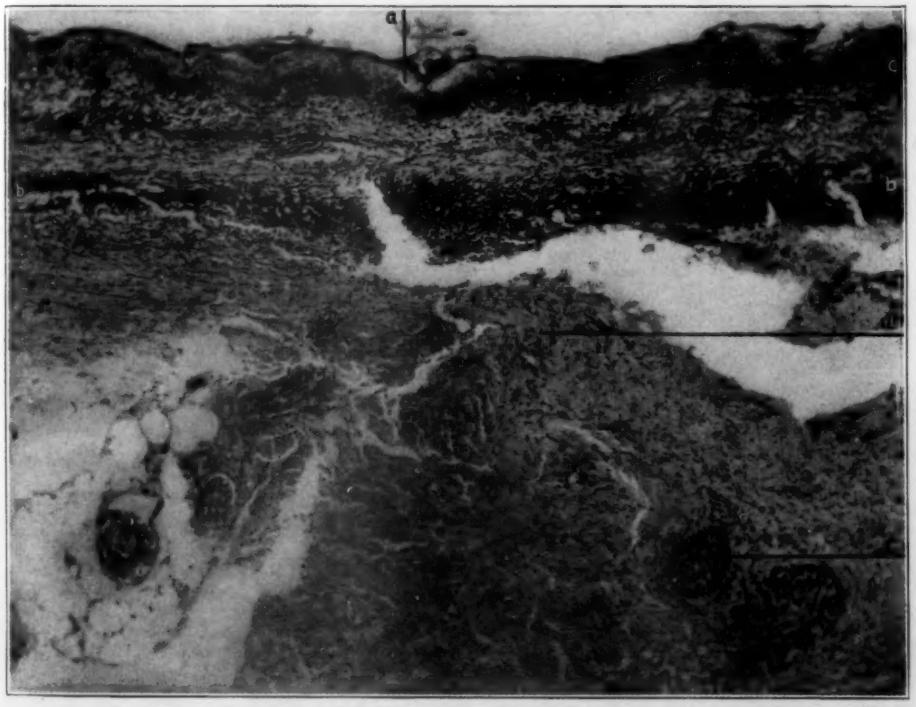

Fig. 2.—High powered view of figure 1. Note the lack of infection beneath the tanned membrane and the excellent condition of the subcutaneous tissue. *a* indicates the tanned membrane; *b*, the junction between the membrane and the connective tissue; *c*, the hair follicles and *d*, the subcutaneous connective tissue. (From Ann. Surg., July, 1926).

toxemia and aids the kidneys. Normal and hypertonic saline administered by hypodermoclysis does much to relieve toxemia and prevent vomiting. Davidson has shown that there is a sodium chloride retention similar to that described by Haden and Orr,[1] and for this reason the use of hypertonic saline may be of great value.

INFECTION BENEATH THE TANNED MEMBRANE

In a typical case of first or second degree burn, after a period of one to two weeks the tanned membrane begins to curl at the edges, and

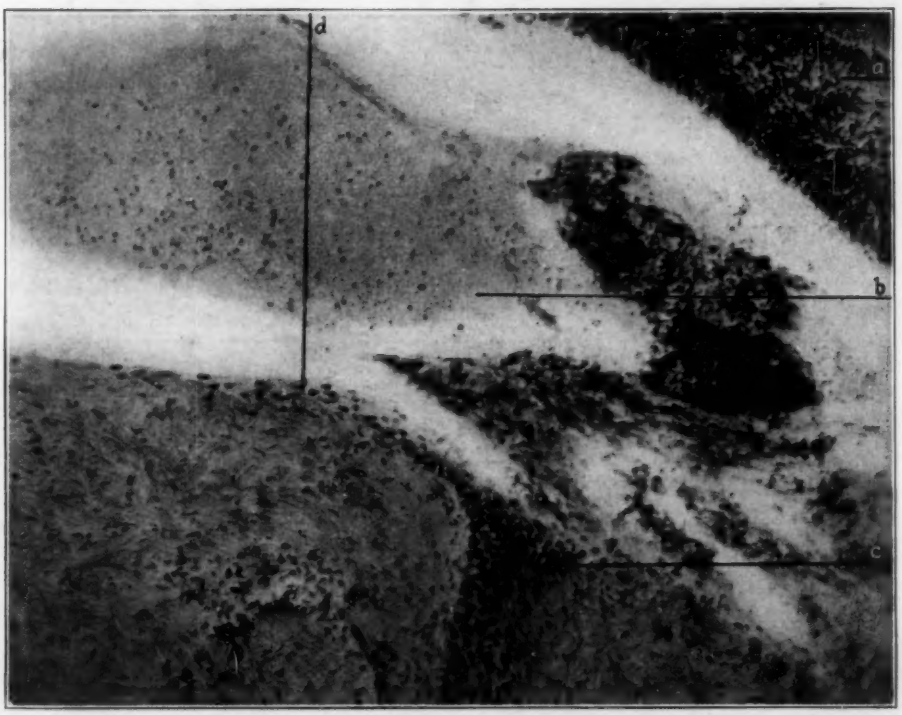

Fig. 3.—High powered view of figure 1. *a* indicates the tanned membrane; *b*, the separation zone; *c*, the hair follicle; *d*, the beginning epithelization arising from the hair follicle, while the tannic acid is in situ.

it is seen that epithelization has already been initiated. If infection is not present, the membrane gradually separates, leaving beneath it newly formed epithelium and granulating areas of relatively small extent, dotted here and there with islands of epithelium (fig. 5).

1. Haden and Orr: Intestinal Obstruction and Gas Bacillus Infection, Surg. Gynec. Obst. **37**:465 (Oct.) 1923; J. Exper. Med. **37**:365 (March) 1923; Bull. Johns Hopkins Hosp. **34**:26, 1923.

Fig. 4.—Area of infection occurring beneath the tannic acid. *a* indicates the tanned membrane; *b*, the separation zone; *c*, the irregular zone of epithelium arising from the hair follicle; *e*, the infection proceeding downward along the hair follicle; *f*, the capillary filled with numerous polymorphonuclear leukocytes showing the gradual spread of infection.

In the third degree type of burns, the membrane is lifted by the serum after a while and has to be removed. Treatment of the granulating surface then presents the same problem as in any third degree burn with any type of treatment. There are a certain number of patients who have an elevation of temperature from 102 to 103 F., which con-

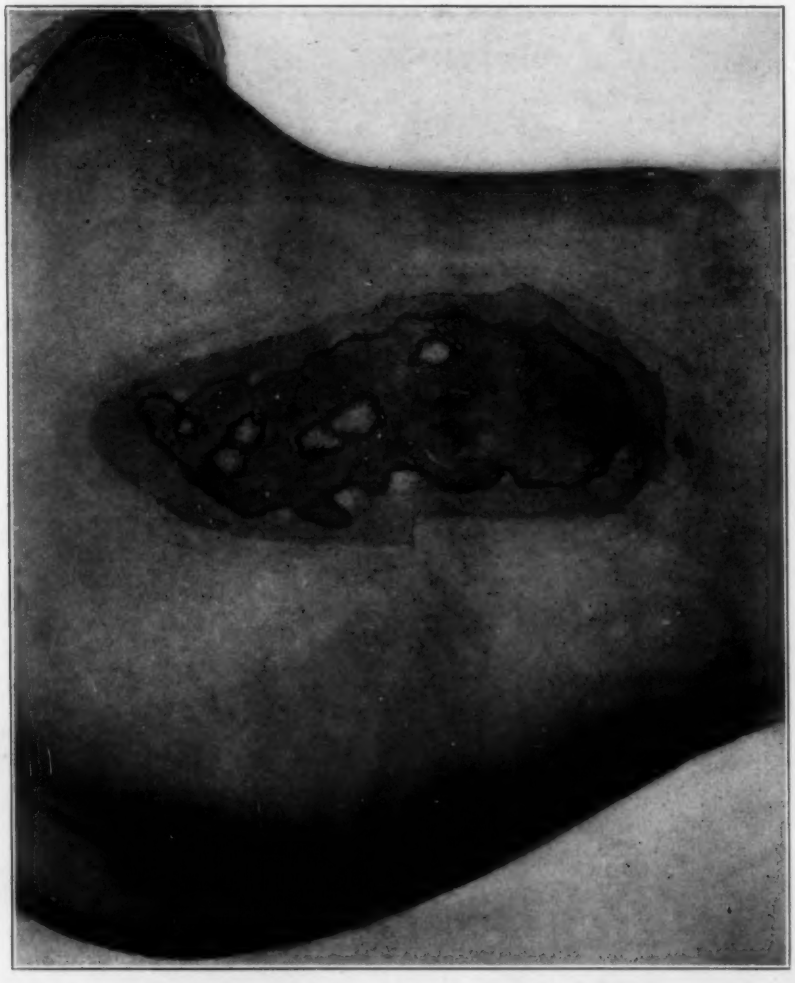

Fig. 5.—Artist's sketch showing the islands of epithelium in the midst of the granulating area following (*a*) tannic acid treatment; (*b*) 1 to 5,000 acriflavine as a wet dressing for the granulating area following the separation of the tanned area.

tinues for a week or ten days; eventually they succumb if the infection is not treated. The pulse is not extremely rapid but of low tension. They do not seem seriously ill. They often suffer from gastro-intestinal

disturbances, such as vomiting and diarrhea. Frequent hypodermoclysis will give them relief from the gastro-intestinal symptoms. Clinically, these cases resemble neither a staphylococcus nor a streptococcus type of infection, but they somewhat resemble a subacute type of gas bacillus infection. During our early experience with burns, a few of these patients died because we did not recognize the necessity of treating the infection beneath the tanned membrane. On studying sections taken from this membrane, we found infiltration of the fat and subcuticular layers with polymorphonuclear leukocytes (fig. 4). After this experience, we decided to treat the patients for the infection and not for the burns. At present, when a patient has a high temperature and there is

Fig. 6.—*A* is the anterior view of the patient in case 1, one year after leaving the hospital. It shows complete extension with no contractures, the result of numerous pinch grafts and the repeated manual extension of the knee joint. *B* is the posterior view of the same patient.

redness about the periphery and tenderness beneath the membrane, it is our custom to anesthetize him and to excise the membrane as far as possible. Wet dressings are then applied to the granulating area. At first, hot boric acid dressings were used. We found that crusts continued to form and that the granulations became infected and exuberant. The epithelization was much delayed.

Bennett, Blackfoot and Browning [2] advised treating these patients with a 1/5,000 acriflavine. We adopted this method and have

2. Bennett, Blackfoot and Browning: Brit. M. J. **2**:306 (Aug. 19) 1922.

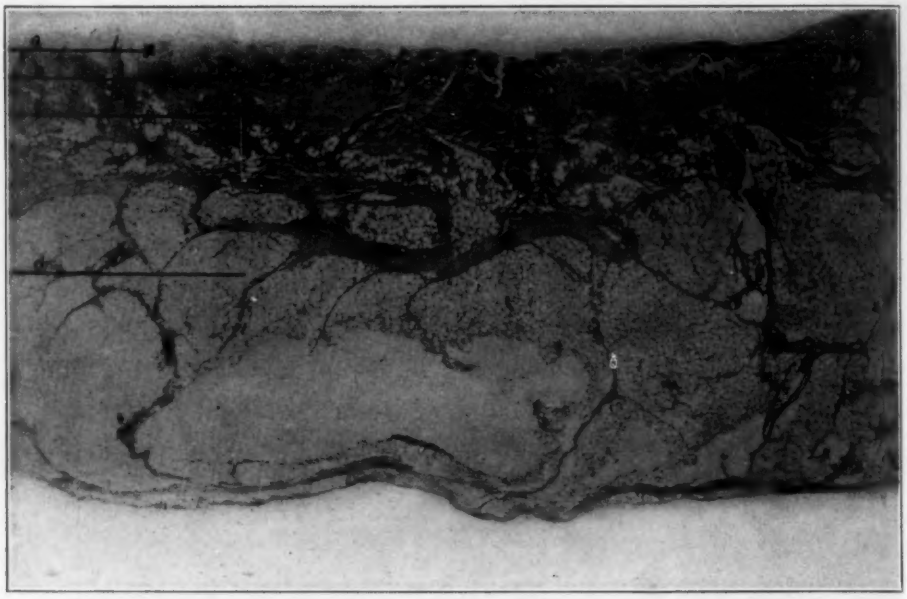

Fig. 7 (case 1).—Low powered view of the tissue debrided six days after the burn. *a* indicates necrotic tissue; *b*, the separation zone; *c*, the living connective tissue and *d*, the fat. (From Ann. Surg., July, 1926.)

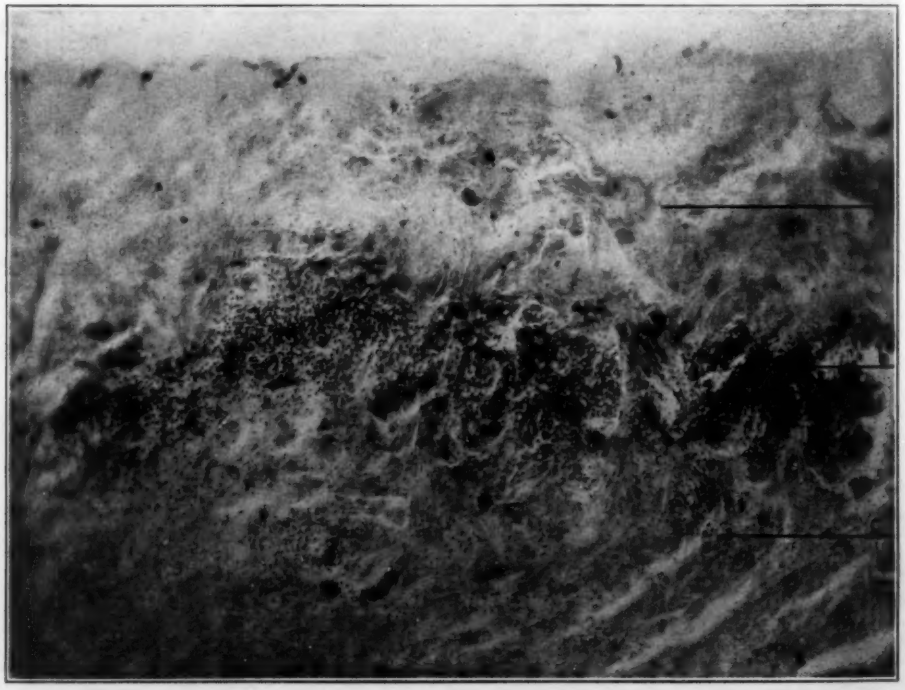

Fig. 8 (case 1).—High powered view of the separation zone; *a* indicates necrosed tissue on the surfaces; *b*, the separation zone; *c*, the connective tissue showing the presence of infection. (From Ann. Surg., July, 1926.)

felt it to be of great value. The dressings are loosely applied and kept saturated with the solution. The granulations beneath it are red and clean, and epithelization occurs rapidly. We have been unable to detect any evidence of toxic absorption from the solution (fig. 5).

In a previous communication (figs. 1, 2 and 3) we have shown that the islands of epithelization that occur beneath the membrane arise from the hair follicles. If infection can be prevented or diminished, this epithelization occurs so rapidly that the necessity for skin grafting has been gradually diminished.

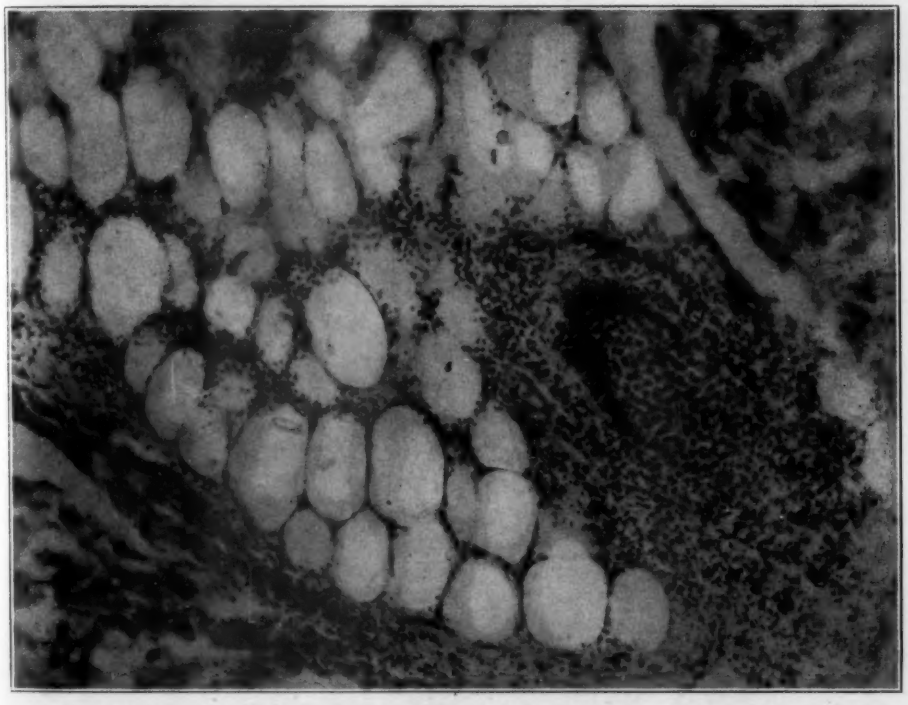

Fig. 9 (case 1).—Deep infection of fat and hair follicles. (From Ann. Surg., July, 1926.)

In areas in which infection of the granulating surfaces has persisted for a considerable time, many failures in grafting the skin occur.

One may assume that so-called exuberant granulation tissue is due to a low grade infection. If this persists, scar tissue forms beneath the superficial granulations. As the scar tissue contracts, the circulation is gradually interfered with, so that unless the entire scar tissue area is removed, skin grafts will not derive sufficient blood supply to persist. If a curet is applied to this area, granulations are scraped off, leaving the scar tissue base, and failure results (figs. 13, 14, 15, 16, 17, 18, 19 and 20).

In children with burns of the extremities we believe that primary attention should be given to the granulating surfaces, and that if contractures tend to occur, daily gentle manual extension by both physician and nurse is preferable to any retention apparatus. After the skin is reformed, an apparatus or operation may be easily devised to overcome the contractures. The following two cases illustrate these factors:

REPORT OF CASES

CASE 1.—V. K., a girl, aged 10, was admitted to the Lincoln Hospital on Jan. 1, 1925, with second and third degree burns caused by hot water over the

Fig 10 (case 2).—Patient four months after admission to the hospital. Note the emaciation of the patient with contractures of the knee joints, swelling and edema of the feet. Figures 14, 15, 16, 17, 18, 19 and 20 are microscopic views of the tissue beneath the granulating areas.

buttocks, thighs, legs, feet and left hand. At this time we had not adopted the treatment with tannic acid. On the sixth day she was intensely toxic and so ill that we doubted that she would live twenty-four hours. Under light anesthesia, the typical pigskin burned area on both thighs was excised down to the fascia (figs. 7, 8 and 9). Wet dressings were then immediately applied. This was followed by a blood transfusion of 250 cc. The next day her condition was markedly improved, and the signs of toxemia gradually disappeared. While she was in the hospital, she received six transfusions and at least ten operations

Fig. 11 (case 2).—Patient two years after admission to the hospital. Note the complete epithelization of the extremities by numerous debridements of the scar tissue followed by pinch grafts; also the scars of the abdomen from which the pinch grafts have been removed.

Fig. 12 (case 2).—Posterior view of complete extension of the right leg. Extension of the left leg is limited by about 20 degrees. There is still an area on the posterior surface which has not completely epithelized.

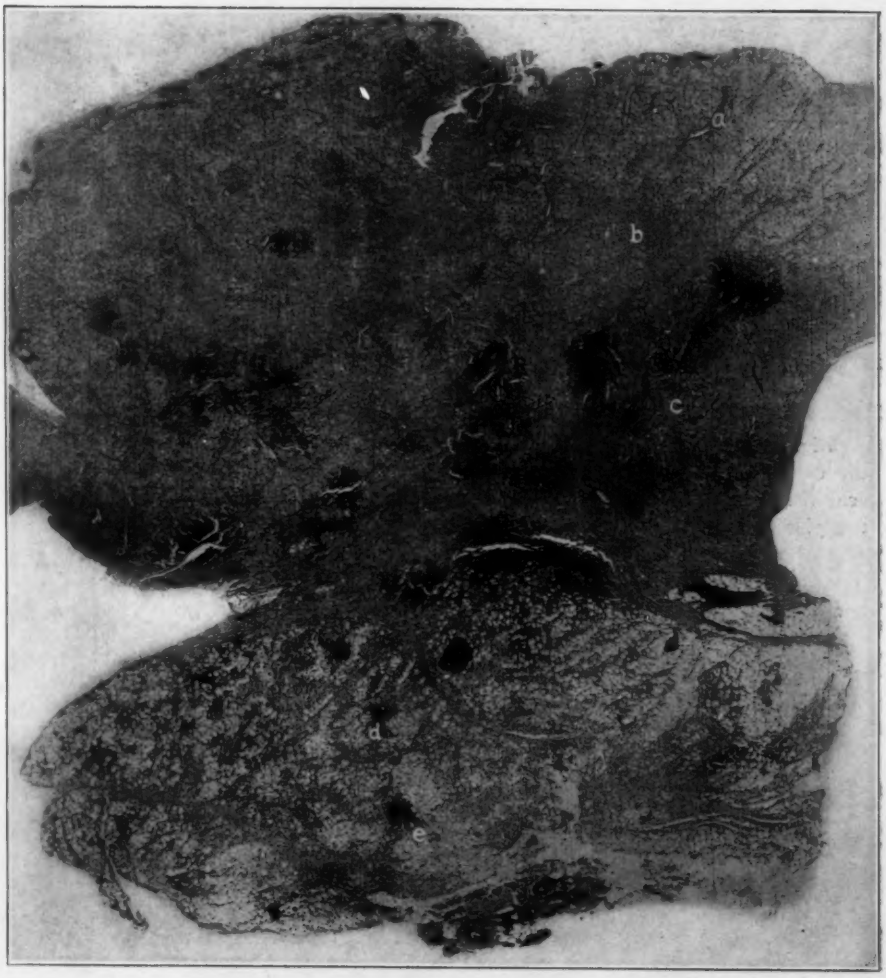

Fig. 13.—Low powered view of the tissues removed by debridement in case 2. *a* indicates the superficial granulating area (fig. 14); *b*, the junction of the granulating area with the scar tissue (figs. 15, 16 and 17); *d*, the deep fat with infiltration of leukocytes and round cells about the vessel (fig. 18) and *e*, infiltration of fat extending down as far as the fascia lata with large cells retaining one or more nuclei (figs. 19 and 20).

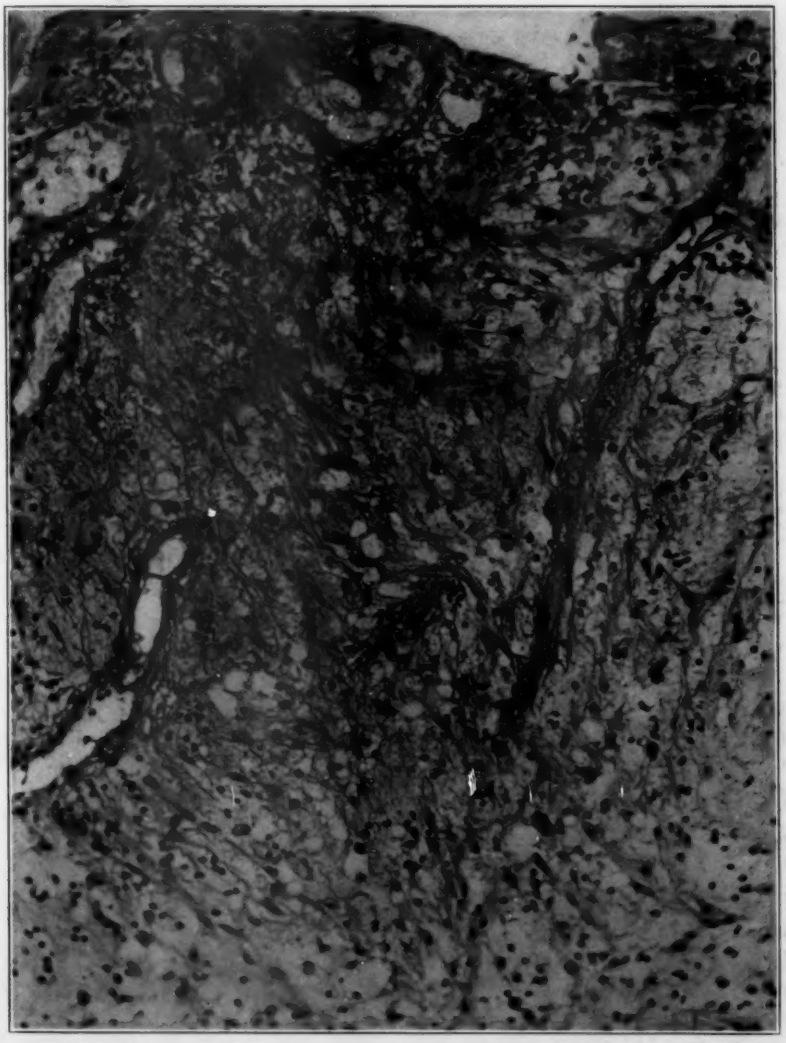

Fig. 14 (case 2).—High powered view showing edema of the superficial granulating area with slight degree of infection. Numerous blood vessels can be seen. *a* indicates the surface.

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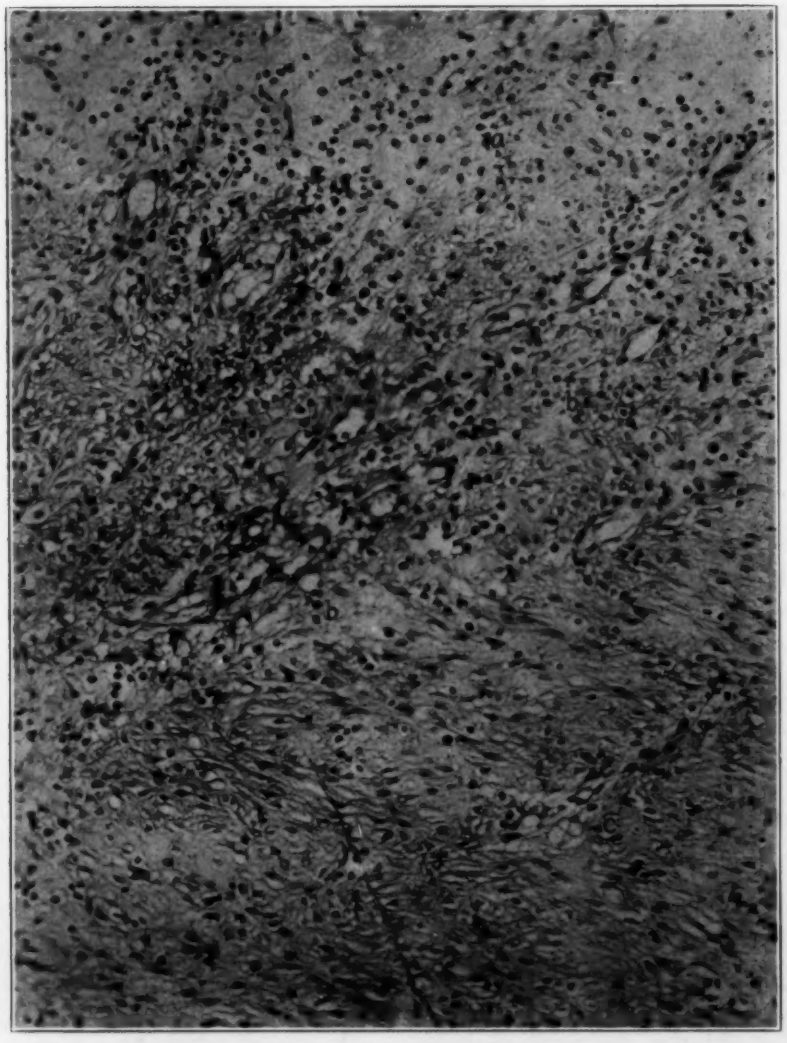

Fig. 15 (case 2).—High powered view of the junction of granulation and scar tissue. *a* indicates the superficial granulation tissue; *b*, the junction of the scar and granulation tissue; *c*, the scar tissue. It is obvious that if a curet were used in this case the granulation would be removed to (*b*), leaving a dense scar tissue base.

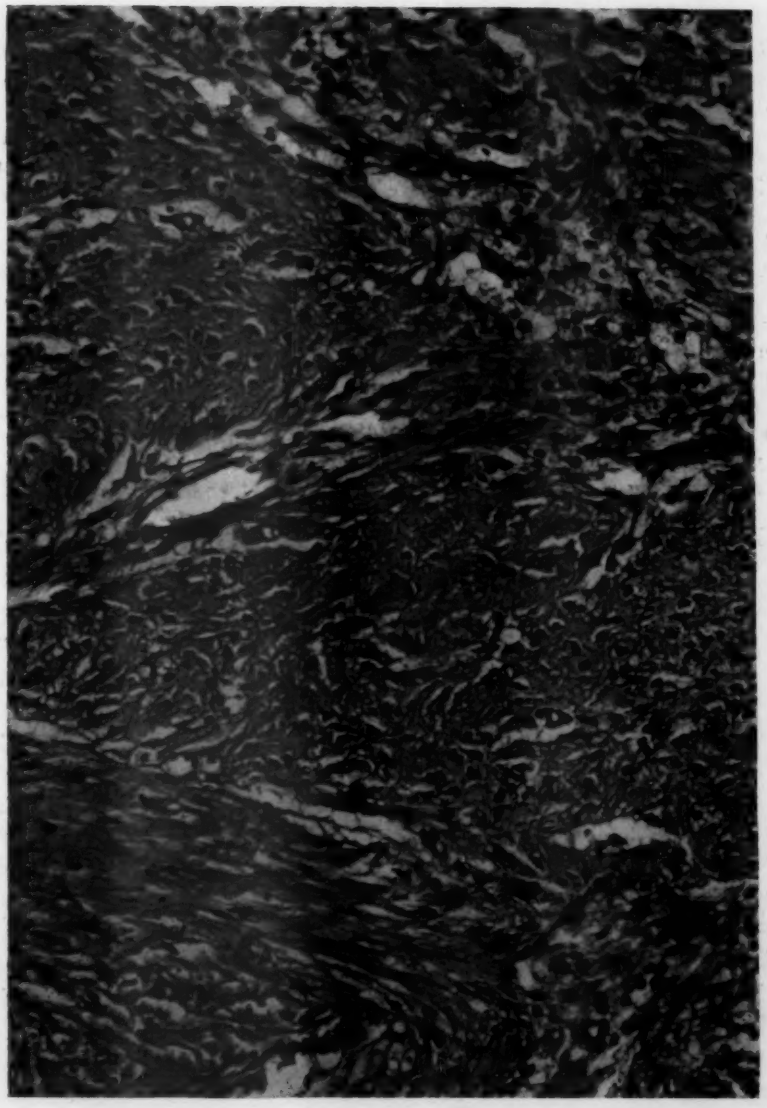

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Fig. 16 (case 2).—Scar tissue beneath superficial granulations.

were performed for skin grafting, pinch grafts being used. She developed moderate contractures of both knees, and after the area was entirely epithelized she was repeatedly taken to the operating room and her legs partially straightened under anesthesia. If the skin tore in the popliteal space, the area was immediately grafted and retentive apparatus applied. This operative procedure was repeated several times, until the contractures were corrected. She is now well, and the flexion and extension in both knee joints is perfect (fig. 6).

CASE 2.—T. T., a boy, aged 3 years, was admitted to the Lincoln Hospital on Nov. 14, 1925. He was extensively burned from the abdomen to 1 inch above the ankle joint. Tannic acid dressings were applied. As the burns were of the third degree type, the membrane gradually separated, leaving extensive granulating surfaces. As he was developing contractures of both knees, it was thought advisable to attempt a Bryant overhead traction, suspending him by stirrups about the feet. Almost immediately he developed pressure sores over the os calcis and the anterior surface of the foot, with resultant edema of the foot and toes (fig. 10). In an attempt to treat the patient for the edema of the foot, grafting of skin on the granulating areas of the thighs was delayed for a long period. Our earliest attempts at grafting skin were failures, although the surfaces had been thoroughly curetted. We then decided that the failure was due to the formation of scar tissue beneath the granulating tissue. Therefore, by sharp dissection, the scar and granulation tissue down to his fascia lata was excised, and skin was immediately grafted on the area. This was followed by success. During the period of two years this child has been subjected to about fifteen operations for skin grafting and numerous transfusions (figs. 11 and 12).

In children with extensive burns who have not much normal skin that can be used for grafts, we have found that pinch grafts can be inserted about 1 cm. from each other, and that epithelization will occur from each graft, bridging the defect. It is better to attempt small areas at a time, repeated operations being performed. The extremity should be immobilized and dressings so applied that there will be no movement of the grafts, and sufficient pressure must be used to prevent the accumulation of serum beneath them. On the other hand, as has been emphasized by Davis, the pressure should not be great enough to interfere with the capillary circulation, so that the grafts may receive their blood supply. We have found it advisable always to excise the scar tissue near the advancing edge of epithelium, because if grafts are planted in the center of the granulating surface, they are gradually choked off by the surrounding exuberant granulating tissues. (Figures 13, 14, 15, 16, 17, 18, 19 and 20 show clearly the pathologic condition in this case.) A curet would have merely scraped off the superficial granulating area and left behind the dense scar tissue base. At one time, the contractures about the knee joints in case 2 were alarming, but by numerous moderate stretchings, with immediate grafting of the rents in the popliteal space and the application of splints to maintain the improved positions, the patient can now completely extend one leg and there is a contracture of only about 30 degrees of complete extension of the other. If we had originally treated the granulating areas to prevent

infection and had grafted them early, the patient's period of hospitalization and disability would have been greatly diminished.

These two cases are presented as contrasts. The child in case 1 was treated primarily by debridement—an inferior method—but skin was immediately grafted, and the contractures were repaired following the

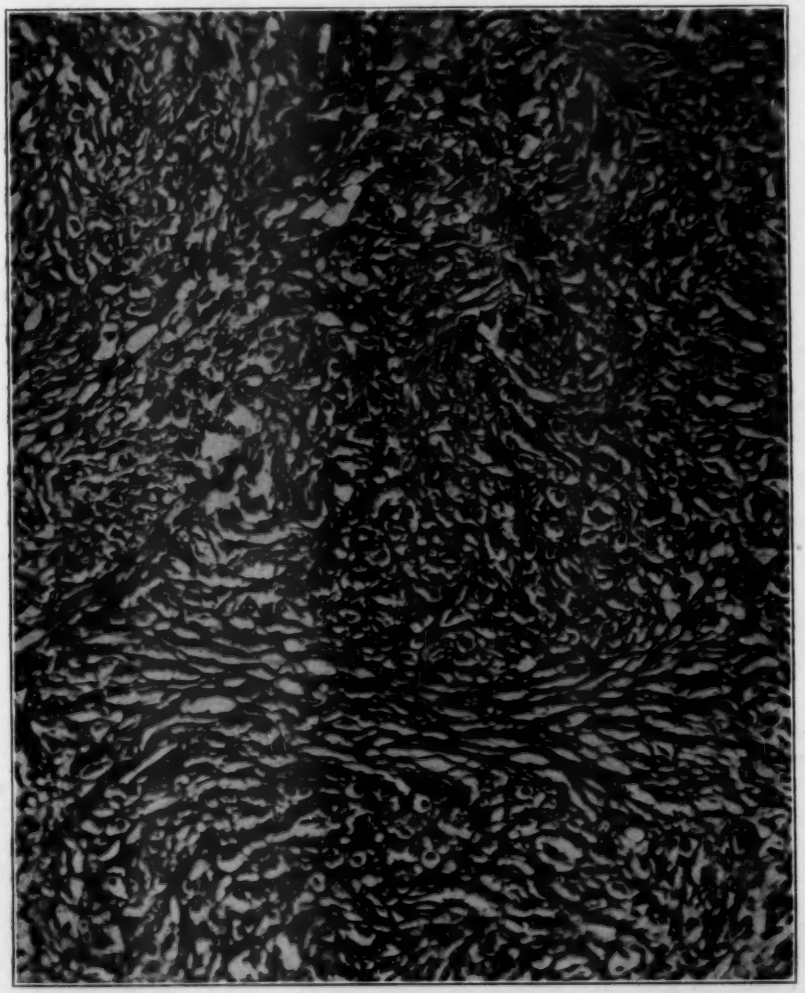

Fig. 17 (case 2).—Dense scar tissue in the region of the deeper area.

epithelization. The child in case 2 was treated by tannic acid—a primarily satisfactory treatment—but in our attempt to prevent contractures, the epithelization of the granulating areas was neglected, and his period of hospitalization and deformity were greatly prolonged thereby.

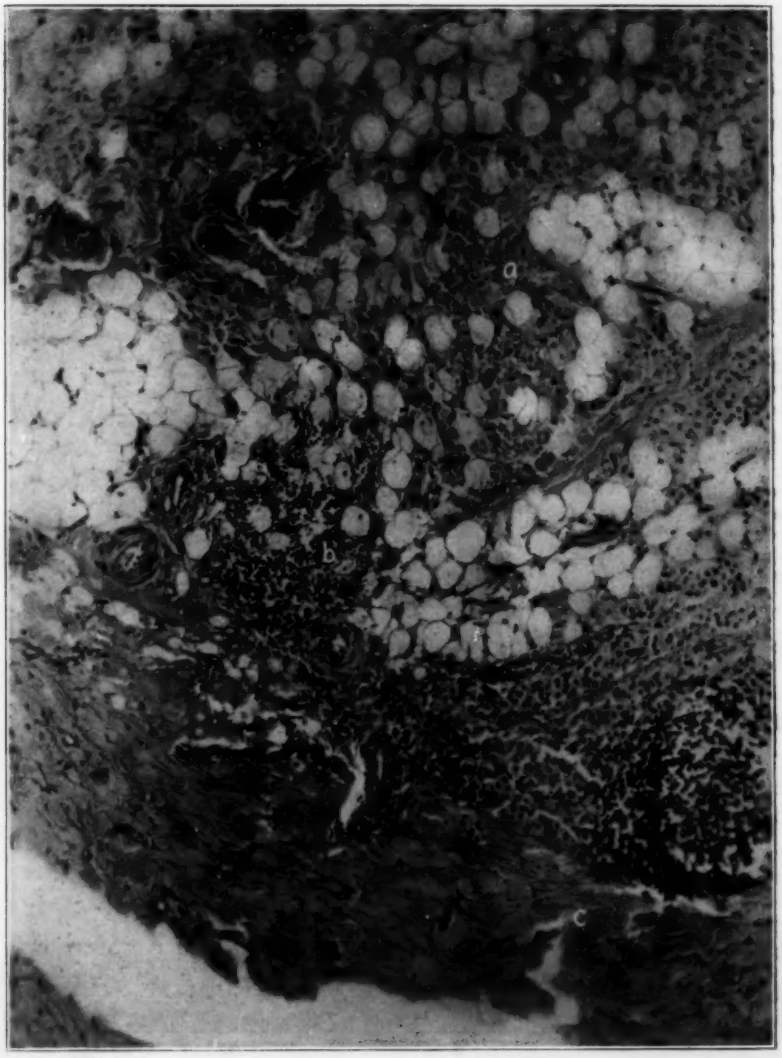

Fig. 18 (case 2).—High powered view of fat showing (*a*) large cells with clear cytoplasm, infiltration of fat; and *b*, perivascular infiltration of leukocytes and *c*, fascia lata.

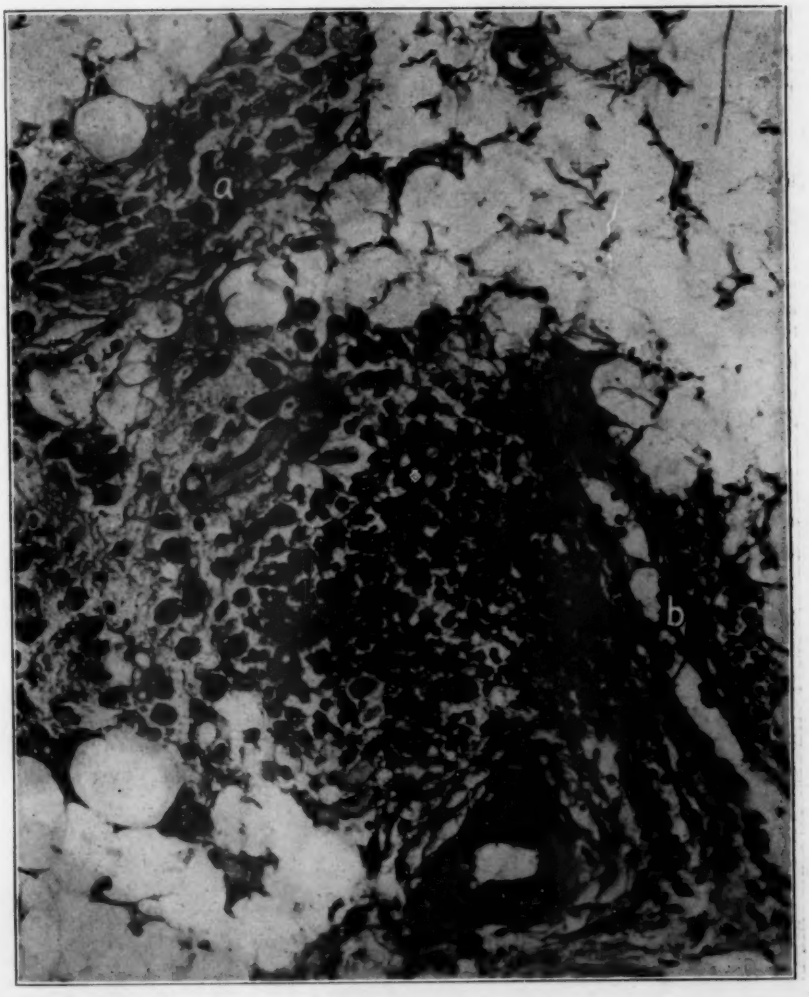

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Fig. 19 (case 2).—Perivascular infiltration of fat with small round cells. *a* indicates the large cells with clear cytoplasm and *b*, the polymorphonuclear leukocytes.

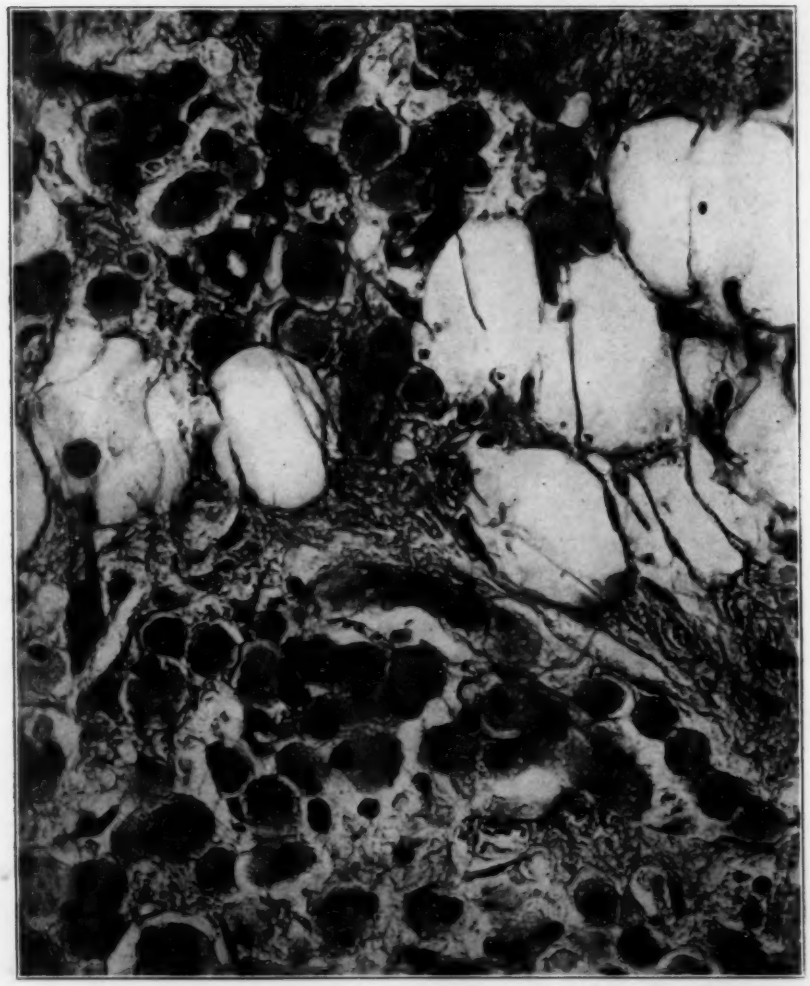

Fig. 20.—High power view of fat showing infiltration with large polymorphonuclear and mononuclear cells with clear cytoplasm. It is obvious from these illustrations that infection extended well below any surface that could be reached by local antiseptics.

CONCLUSIONS

1. Infection frequently occurs beneath the tanned membrane.

2. If infection occurs, debride the eschar and treat the underlying cellulitis.

3. Acriflavine 1/5,000, applied as a wet dressing, tends to diminish infection and apparently aids the epithelization.

4. In deep third degree burns, it is advisable to apply skin grafts soon after the sloughs separate.

5. When granulating areas have been infected and there has been a delay before grafting is attempted, it is advisable to excise the scar tissue down to the underlying fascia. Pinch grafts immediately applied are usually successful.

METASTATIC OPHTHALMIA

SUBACUTE ENDOCARDITIS COMPLICATED BY METASTATIC OPHTHALMIA AND MENINGITIS; DISTRIBUTION OF GENTIAN VIOLET SOLUTION SIX AND ONE-HALF HOURS AFTER INJECTION INTO CISTERNA MAGNA. REPORT OF A CASE *

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SAN FRANCISCO

Metastatic ophthalmia usually means an inflammation of the eyeball, resulting from some endogenous infection. This inflammation takes place through an embolus; septic material from some focus of suppuration enters the circulation and becomes lodged in the choroidal vessels. The cases vary; the infection may be mild, a small degree of sight being retained, or, as in cases of severe infection, the condition may resemble panophthalmitis. One or both eyes may be affected. According to Fuchs,[1] in rare instances, this condition may occur in acute infectious diseases, such as typhus and typhoid fever, variola, scarlet fever, anthrax, influenza, ulcerative endocarditis, diphtheria, erysipelas, pneumonia and Weil's disease. Metastatic ophthalmia is produced either by ordinary germs, among which the streptococci rank first and the pneumococci second, or by bacteria which are specific for certain definite diseases (e.g., the meningococcus, the pneumobacillus, the influenza bacillus, the typhoid bacillus or other bacteria). A mixed infection may also occur.

REPORT OF CASE

History.—F. W., a man, aged 63, was first seen at the Stanford University Eye Clinic on March 31, 1926. Five years before coming to the clinic, he had been struck in the right eye with an iron pipe, and a foreign body had been removed from the cornea. Since then the eye had become inflamed a number of times, the inflammation lasting a week. He was not sure whether the vision was impaired following the inflammations. The present complaint was that his right eye had felt "sandy" and painful for two days, and that he was unable to see with it.

Examination.—The patient could see fingers at a distance of 10 feet (304.8 cm.) with his right eye; glasses did not improve the sight. With his left eye he could perceive movement of the hand; with a -5.0 spherical lens, this vision was 15/15. Examination of the right eye showed a steamy, gray cornea; a moderate palpebral and bulbar conjunctival injection, and small pupil. The media and fundus were not seen, owing to the opacity of the cornea. There was a hypopyon, 2 mm. high, with a number of blood vessels leading from the sclera toward the

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* From the Department of Ophthalmology, Stanford University Medical School.

1. Fuchs, E.: Text-Book of Ophthalmology, ed. 7, Philadelphia, J. B. Lippincott Company, 1923, pp. 98 and 718.

hypopyon. The left eye was normal, with the exception of a nuclear cataract. The patient appeared more ill than could be explained by the condition of the eye. He was admitted to the hospital for observation and treatment.

The previous history was negative, and a history of a present systemic complaint was not elicited. Physical examination showed that the teeth were in poor condition and that pyorrhea was present. The throat was clear; the neck showed pulsating vessels, but adenopathy was not found. The expansion of the chest was equal but poor. The heart did not show any increase in size; the apex was in the fifth intercostal space, 7 cm. from the midsternal line. The right border of cardiac dulness was not increased, and the supercardiac dulness was 6 cm. The sounds were distant but clear, and murmurs were not heard. The lungs were hyperresonant. There was bronchovesicular breathing, and coarse sonorous râles were heard throughout; there was no abnormal dulness, and moist râles were not heard.

Examination of the abdomen revealed dulness of the liver from the fourth right costal space to the umbilicus. The liver was smooth, and a nontender edge was readily felt 12 cm. below the right costal margin in the right midclavicular line. The spleen and kidneys were not felt. Tenderness or evidence of fluid was not found. The knee jerks were sluggish, and the ankle jerks were not obtained. The blood vessels were thickened; the radials were equal, synchronous and regular. The blood pressure was 92 systolic and 38 diastolic. The temperature was 39.2 C. (103.8 F.); the pulse rate, 100, and respiration, 24. The white blood cells numbered 10,050; polymorphonuclears, 80 per cent, and lymphocytes, 20 per cent.

Treatment and Course.—The patient received 15 cc. of milk parenterally. The next morning he said that his eye felt better. The cornea was duller and yellowish. There was a yellow ring on the posterior surface of the cornea a few millimeters from the limbus, giving the appearance of a ring abscess. The hypopyon was of the same height, but the eyeball was intensely injected. The temperature varied between 37.2 and 38.2 C. (98.9 to 100 F.). The pulse rate and respiration were normal. The white blood cells numbered 23,700; polymorphonuclears, 93 per cent, and lymphocytes, 7 per cent. The patient felt chilly.

On the following morning, marked chills developed; the patient trembled and was irrational. There was marked rigidity of the extremities with occasional complete relaxation and a great deal of muscular twitching. All the deep reflexes were present and equal. Kernig's and Brudzinski's signs were positive. There was also involuntary passage of urine. The rectal temperature varied between 40.2 and 40.8 C. (104.3 and 105.4 F.); pulse rate, from 88 to 100, and respiration, from 20 to 28. The blood pressure was 138 systolic and 70 diastolic. The white blood cells numbered 14,900; polymorphonuclears, 92 per cent, and lymphocytes, 8 per cent.

Within twenty-four hours, the bulbar conjunctiva became edematous and the eye was bulging. There was little to be seen of the cornea. The diagnosis of meningitis and panophthalmitis (metastatic ophthalmia) was made.

A spinal puncture was performed with the following results: pressure, 39 cm.; cells, 98; leukocytes, 98; Nonne test, +++; Noguchi test, +++. The Wassermann reaction of the blood and spinal fluid was negative; urinalysis was negative.

Smears of centrifugalized spinal fluid, stained with methyl violet, showed many incapsulated streptococci occurring in long and short chains, and as diplococci. There were many pus cells. A blood culture showed a growth of hemolytic streptococci.

A lumbar puncture needle was inserted between the second and third lumbar vertebrae. A second needle was inserted into the cisterna magna, and 30 cc. of

spinal fluid was drained off. Twenty cubic centimeters of saline solution was injected into the cisterna, followed by 35 cc. of 0.25 of 1 per cent gentian violet. The gentian violet appeared at the lumbar needle in about ten minutes. During the foregoing procedure, the patient's pulse became rapid, weak and thready, but he recovered promptly.

The patient died during the night, fifty-three hours after his admission to the hospital, and six and one-half hours after the injection of gentian violet.

Clinical Diagnosis.—The following clinical diagnosis was made: Metastatic ophthalmia; streptococcic meningitis.

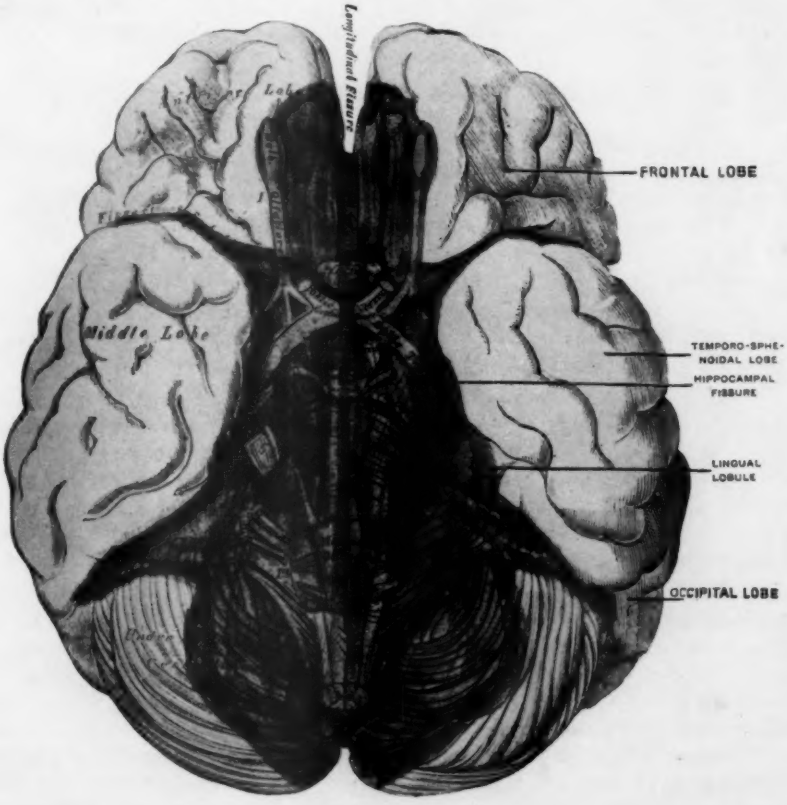
Anatomic Diagnosis.—The anatomic diagnosis was as follows: Subacute endocarditis of the aortic valves with valvular aneurysm; acute, streptococcic meningitis; streptococcic panophthalmitis; early carcinoma of the stomach; syphilis of the aorta; syphilis of the liver; syphilitic cirrhosis; fatty liver; hydrocele; emphysema; apical tuberculosis of the lungs, healed; mucopurulent bronchitis.

Summary of Necropsy Record.—A necropsy was performed by Dr. Ophüls, and the following observations were made: The man was strongly built and moderately well nourished. There was marked cyanosis of the face and neck; the superficial lymph glands were not enlarged. Edema was not present. There was marked chemosis. The conjunctiva of the right eye was greatly congested and contained a small amount of pus. The cornea showed a ring-shaped infiltration with pus along the edge of the ring; the corneal surface did not show any visible defect.

The skull cap and the longitudinal sinus were normal. The meninges on the right side were congested, edematous and showed moderate infiltration with pus, especially beside the sagittal fissure and along the course of the large blood vessels. The pia mater at the base of the brain was intensely stained with gentian violet. The dye coloring covered the median side of the frontal lobes to the edge of the olfactory bulbs and had penetrated a short distance into the sylvian fissures, as shown in the illustration. It had stained the entire base, including the pons, medulla and the median part of the lower surface of the cerebellum. The lower surface of the occipital lobes and the upper surface of the cerebellum were free. There was a slight purulent infiltration of the meninges over the lateral part of the cerebellum. The gentian violet appeared to be largely in the subarachnoid space. There was a small amount of the dye on the upper surface of the cerebellum near the posterior end of the fornix. Both lateral ventricles were intensely stained with the dye. The dura mater at the base of the brain from the region of the pituitary body to the rounding of the foramen magnum and also the anterior part of the tentorium were stained with gentian violet. The upper surface of the pituitary body was stained with the dye which did not penetrate into it. The proximal end of the sheaths of the ocular nerves was also stained with the dye. The gentian violet did not penetrate the orbits. Pus had not accumulated along the course of the optic nerves. The tissue of the orbits were free from infection.

The teeth of the lower jaw were in bad condition. The chest was large, deep and symmetrical. There were some old broken adhesions in the upper part of the pleura of both lungs. The left lung was diffusely emphysematous. There was a small superficial scar at the left apex. The bronchial tubes were dry, and those of the lower lobe contained a little mucopurulent material. The posterior part of the left lung was congested and edematous. A similar scar was found at the right apex, with a bullous emphysema. The congestion of the right base was more marked. The peribronchial lymph nodes were normal on both sides.

About 50 cc. of clear fluid was found in the pericardium. The heart was small and the heart muscle was soft and flabby. The heart valves were normal, except the aortic cusps. Two of these showed slight roughness along the edge. The third one showed destruction at the base with the development of a valvular aneurysm about 2 cm. in diameter, which had perforated. The opening of the perforation measured about 1 cm. The base of the aorta showed marked scarring, and was distinctly and irregularly dilated. The coronary arteries were normal. The heart muscles on the right side averaged 2 mm.; on the left, 10 mm. Scars or areas of degeneration were not visible.



Base of the Brain.

Fig. 1.—Diagramatic presentation of the distribution of gentian violet solution staining the base of the brain.

The spleen was large, measuring 16 by 12.5 by 4.5 cm. The capsule was slightly thickened and the splenic tissue was dark, red and soft. The kidneys showed some edema of the perirenal tissue and a few scars in the cortex. They measured 13 by 6 by 3.5 cm. and were congested and edematous. The bladder and seminal vesicles were normal; the prostate was small. The rectum contained much pus, but otherwise was normal.

The stomach contained some stained mucus. At the lesser curvature, about 3 cm. from the cardiac orifice, there was a flat, infiltrating, white tumor, about

5 cm. in its largest diameter. The regional lymph nodes were not involved. The pancreas was normal. The liver projected three fingerbreadths in the right midclavicular line and was irregularly and deeply lobulated; it measured 28 by 23 by 8 cm. The capsule on the convexity was irregularly thickened and the liver tissue was nodular. The cut surface was slightly nodular. There were a few visible strands of fibrous tissue and some large scars at the base of the coarser lobulations. The gallbladder and contents were normal. The mesentery of the sigmoid flexure was cicatrized and contracted.

In the thoracic lumbar aorta, there was a moderate number of yellowish atheromatous plaques; there was also some scarring at the beginning of the aorta. The marrow of a rib was plentiful and soft. The tunica vaginalis of the right testis was filled with clear fluid and distinctly thickened. The testes showed moderate atrophy.

Histologic Examination.—Examination of the aorta showed marked irregular fibrous thickening of the intima with fatty degeneration, necrosis and calcification encroaching somewhat on the media. There was old diffuse fibrosis of the media, marked fibrous thickening of the adventitia with endarteritis of the vasa vasorum and moderate round cell infiltration about them. The mucous membrane of the stomach showed marked atrophy. In the liver there were some irregular strands of new fibrous tissue with moderate round cell infiltration; also moderate fatty infiltration. The rest of the liver tissue was normal. The pulp of the spleen was extremely congested; the arteries were normal. The lungs showed moderate emphysema and marked congestion. A smear of the marrow showed many polymorphonuclear leukocytes; otherwise, apparently it was normal.

Bacteriologic Examination.—There were many red cells in the aortic cusps; few leukocytes and many gram-positive diplococci and streptococci in short chains. Many leukocytes and rather long chains of delicate gram-positive diplococci were seen in the meninges. Examination of the conjunctiva showed many epithelial cells and leukocytes, but bacteria were not present. Neither leukocytes nor bacteria were found in the orbital fat. The spleen showed many leukocytes, but no bacteria.

Examination of the Eyeball.—Macroscopic: The eye was hardened in a solution of formaldehyde. The vitreous contained a large amount of yellowish pus. The lens lay free against the vitreous with a black pigmented ring on its anterior capsule. There was pus in the anterior chamber. The cornea was opaque, thickened and yellowish, and the posterior surface had a depression 3 mm. wide and 3 mm. from the limbus, forming a ring abscess. The central part of this surface, about 4 mm. in diameter, was also depressed and flat. Between this central depression and the ring abscess the corneal surface was covered with linear striations. The anterior surface of the cornea was smooth, opaque and yellowish white. The ring abscess viewed from the anterior surface appeared as a dirty yellow ring. Adhesions were not found between the iris and the cornea, nor between the iris and the lens. The retina, sclera and ciliary body were easily separated from the choroid. The sclera was normal in appearance and separated freely from the conjunctiva. The optic nerve, 4 mm. long, did not show any abnormality, and its sheath was normal.

Histologic: Histologic sections of the eyeball were stained by the hematoxylin-eosin method and examined by Dr. Swett. There was a marked chemosis at the limbus with areas of round cell infiltration and multiple small hemorrhages. The cornea was swollen, and, except for a small margin near the limbus, showed an absence of epithelium. There was a raised area, about 1 mm. wide and approximately 3 mm. inside the limbus, in which the stroma of the substantia propria

was separated by edema, and Bowman's membrane was ruptured and in places destroyed. The corneal tissues within this area were either poorly stained or absent, especially in the deeper layers near Descemet's membrane which was still intact. Beneath the raised surface, near the limbus, the whole thickness of the cornea, especially just above Descemet's membrane, was densely infiltrated with round cells, forming a line of demarcation 2 mm. from the limbus. There was a heavy deposit of fibrin, polymorphonuclears and pigment over the posterior surface of the cornea.

Examination of the uvea showed that the iris was poorly stained, with pyknosis and an occasional small hemorrhage near the root. The sphincter could not be seen and the pigment layer was gone. The ciliary body was engorged, and full of hemorrhages and round cell infiltration, its surface being covered by a heavy deposit of exudate, which in this region extended into the vitreous. The choroid was engorged and showed a beginning cellular infiltration which was more marked anteriorly.

The retina was still in situ, but there was an increasing amount of necrosis from the disk, where it appeared practically normal, toward the pars ciliaris. The anterior two-thirds of the retina was thin, atrophic and necrotic, and was covered by areas of exudate. The disk was normal except for slight edema.

The lack of inflammatory changes in the posterior portion of the choroid and retina showed that the process was so virulent that necrosis was complete before there was any inflammatory reaction.

Bacteriologic: The slides stained by the Gram-Weigert method showed considerable purulent exudate over the retina and choroid, and infiltrating the cornea. There were many groups of gram-positive diplococci, some in short chains, scattered through the exudate, especially in the region of the ciliary body and the anterior chamber.

Diagnosis: The diagnosis was: Metastatic endophthalmitis, septic; ring abscess of the cornea.

COMMENT

A case is reported in which a patient had subacute endocarditis of the aortic valves which was not diagnosed during life. The condition was complicated by an infection of the eye, later diagnosed as metastatic ophthalmia, and by meningitis. Metastatic ophthalmia due to ulcerative endocarditis is rare. According to Osler,[2] the following figures give the approximate estimate of the frequency with which different parts of the heart were affected in 209 cases of malignant endocarditis: aortic and mitral valves together, 41; aortic valves alone, 53; mitral valves alone, 77; tricuspid, 19; the pulmonary valves, 15, and the walls of the heart, 33. Acute suppurative meningitis was encountered in five of his twenty-three Montreal cases, and in over 10 per cent of the 209 cases analyzed in the literature.

The causative organism, streptococcus, was found during life in the centrifugalized spinal fluid as encapsulated streptococci occurring in long and short chains, and as diplococci; a blood culture showed a growth of hemolytic streptococci. Bacteriologic examination of the

2. Osler, W.: The Principles and Practice of Medicine, ed. 10, New York, D. Appleton & Company, 1925, p. 818.

aortic cusps, at necropsy, showed many gram-positive diplococci and streptococci in short chains; of the meninges, many rather long chains of delicate gram-positive diplococci, and of the eye, many groups of gram-positive diplococci, some in short chains.

Just what the injury to the right eye, which the patient received five years before, and the recurrent inflammations had to do with the present infection is hard to say, except that it offers a hypothesis that an eye previously injured and subject to inflammations was more susceptible to an endogenous infection than it would have been otherwise.

In addition to the unusual conditions found at necropsy, there was the extensive staining obtained by the injection of 35 cc. of 0.25 of 1 per cent gentian violet into the cisterna magna. The dye had stained the entire base of the brain, including the pons, the medulla and the median side of the frontal lobes to the edge of the olfactory bulbs and the median part of the lower surface of the cerebellum. The gentian violet appeared largely in the subarachnoid space. A small amount of the stain was found on the upper surface of the cerebellum, near the posterior end of the fornix. The dura mater at the base of the brain from the region of the pituitary body to the roundings of the foramen magnum and also the anterior part of the tentorium were stained with the gentian violet. The upper surface of the pituitary body was stained with the dye which did not penetrate into it. The proximal end of the sheaths of the ocular nerve was also stained. The gentian violet did not penetrate the orbit.

SUMMARY

A case of metastatic ophthalmia and meningitis of streptococcic origin, with complications of subacute endocarditis is presented, in which diagnosis of the endocarditis was not made during life.

The causative organism, the streptococcus, was found during life in the spinal fluid and in a blood culture and at necropsy in the aortic cusps, the meninges and the eye.

Gentian violet, which was injected into the cisterna magna six and one-half hours before the patient's death, was found to have stained the base of the brain extensively, a great deal of it appearing in the subarachnoid space.

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LIVING SUTURE GRAFTS IN THE REPAIR OF FRACTURES AND DISLOCATIONS*

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The use of transplants of fascia lata in the repair of defects in the soft parts, as advocated by Gallie and Le Mesurier, has created a widespread interest in the use of living tissue as suture material. Many surgical conditions, especially recurrent and large direct hernia, are now satisfactorily dealt with by this method. Massive grafts had been used before and reconstruction of tendons accomplished; however, marked general use of the material had not come into vogue before the experimental and detailed clinical work of Gallie and Le Mesurier became known. There are now frequent reports on the use of this material for the correction of recurrent dislocations and repair of ligaments. A simple method for using massive transplants of fascia lata in the repair of certain acute lesions of the bone and joint is described here. Osgood and Bucholz have shown that tendons passed through drill holes in bone rapidly become firmly attached to the bone and form a solid living ligament. It has also been demonstrated that fascia will become adherent to fascia and that these transplants live to take over the function for which they are intended. The tensile strength of the material is greater than one might expect, and though it varies somewhat, depending on the person from whom it is taken, it can be relied on in certain widths to maintain its position under the necessary strain on it to a degree that equals in efficiency any of the metallic materials in common use.

LUXATION OF THE STERNOCLAVICULAR ARTICULATION

This condition is apparently rare, only five cases having been observed in a period of eight years. It is usually produced by a fall, striking on the point of the shoulder. Four of the five cases have occurred in young males. The lesion is characterized by an undue prominence over the inner end of the clavicle, which becomes more marked on abduction and external rotation of the arm, the displacement being upward. When the arm is lowered to the side, the clavicle can often be seen and felt and sometimes heard to click into place. This maneuver is associated with pain and makes the patient avoid abduction as much as possible. Roentgen-ray examination often fails to reveal the lesion clearly when the plates are taken in the ordinary way. The best results are obtained by a comparative study of both sides with the arms abducted.

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* From the Fracture Service of the Massachusetts General Hospital.

Long periods of fixation with the arms to the side (three months in one case) did not result in a permanent reduction, the luxation taking place on the first attempt at abduction of the arm. There are some luxations of the sternoclavicular articulation that do not result in recurrent or permanent deformities. Posterior dislocation has been observed in the case of a school boy, aged 16. The tendency to upward displacement after reduction was not noted as in the other cases. Dr. William Darrach has called my attention to certain upward dislocations that have healed spontaneously, and suggests, in explanation, the possibility of a rupture of the rhomboid ligament in the cases in which recurrent luxations take place. This is probably what occurs, although in the patients operated on so far we have neglected to examine this

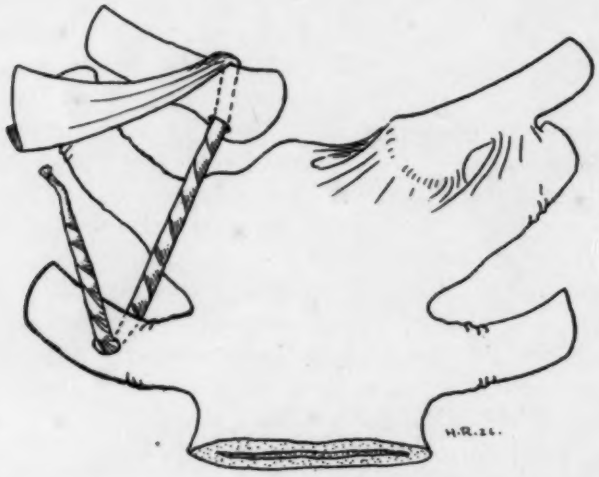

Fig. 1.—Diagrammatic representation of the luxated sternal articulation of the clavicle. The inner end of the clavicle has been drilled vertically and the second rib anteroposteriorly. The fascial graft has been passed through. The method is advocated in children and adults of short stature. The graft was 2 cm. by 20 cm.; the drill, 3 mm.

ligament particularly. The impression has been gained at operation, however, that no ligamentous attachments in this region are intact. Darrach bases his theory on the proved rupture of the coracoclavicular and conoid ligaments in certain dislocations of the outer end of the clavicle and certain fractures through the outer 3 cm. of this bone. In the recurrent cases, we have felt that a repair is unpractical without the introduction of some material for internal fixation. At first sight it seemed reasonable to suppose that a loop of wire or fascia lata might be placed around the inner end of the clavicle and the first rib. It was found, however, that this portion of the first rib could not be safely

exposed, due to its depth and to the great vessels underlying it. In two of these cases, occurring in boys aged 15 and 16, the second rib was found to be suitably deep, anteroposteriorly, and easily accessible. The clavicle was drilled vertically just lateral to the articular surface with a 3 mm. drill and the second rib fenestrated just lateral to the costal cartilage from front to back. A silver probe was passed through these drill holes, followed by a strand of strong silk to which was attached a strip of fascia lata 2 cm. in width and 20 cm. in length (fig. 1). The ends of the fascia were then spread out and the lower portion fenestrated by a longitudinal slit, about 1 cm. in length, placed approximately 5 cm. from the end. The upper portion of the fascia was passed through this slit, the clavicle snugged into its articulation and

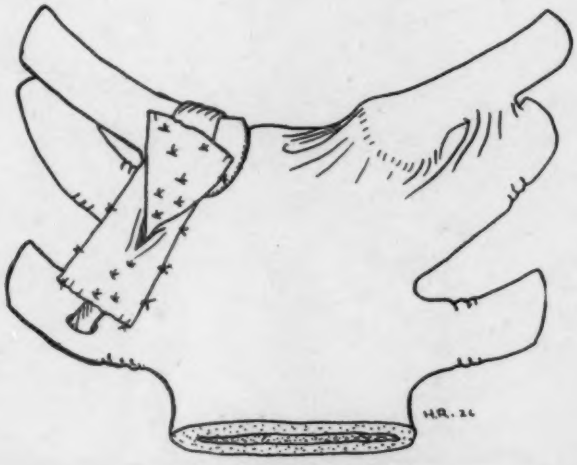

Fig. 2.—Completed fixation of the luxated inner end of the clavicle. The fascial graft has been fanned out, the lower end passed through the upper, and fastened to itself and surrounding structures with multiple chromic catgut no. 0 sutures.

the new ligament fixed to itself and surrounding tissue by many interrupted chromic catgut O sutures (fig. 2).

In one of the patients, a tall adult, aged 20, the second rib was found to be so far below the luxated joint that the ligament would have been long, and for fear of failure or discomfort to the patient, due to its length, the sternal articulation was drilled (figs. 3 and 4). In this case, as in the two adolescent youths, the end-result was satisfactory. There was no tendency to luxation of the clavicle, even on violent abduction of the arm. It seems less hazardous, however, to drill through the bony portion of a rib than through the cartilagenous surface of the sternum, and the former method is the one of choice when feasible.

The fourth case observed was that of a child, aged 8, who had extensive pulmonary tuberculosis; operation was not attempted. A fifth case has been seen recently in a thin young woman, aged 18, who was injured in an automobile accident three months prior to examination. A typical deformity was present. There are no symptoms except discomfort on abduction of the arm. She is able to do her work, which is clerical. Her chief complaint is the deformity, and she is still undecided as to whether a scar in this region would be preferable to the present appearance.

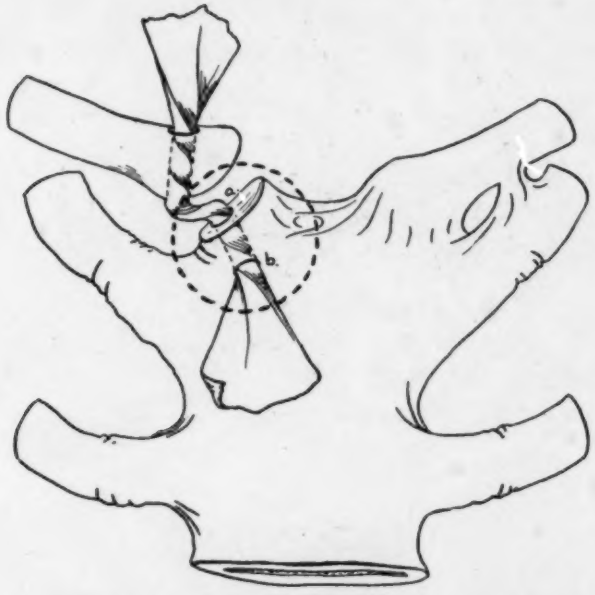

Fig. 3.—Method of fixing clavicle by drilling the sternal articulation.

FRACTURE OF THE PATELLA

In this rather common fracture in which operation is the usual procedure, the use of a massive graft of fascia lata seems to be the ideal method of repair. It is desirable to obtain close, accurate and permanent apposition of fragments in such a manner that early motion of the knee joint can be allowed. The end-results by most of the accepted methods of suture are usually good, whether obtained by repair of the capsule and lateral extension tear with chronic catgut or kangaroo tendon or by wiring the fragments together. The capsular suture alone, however, is prone to result in poor approximation of fragments and necessitates several weeks of fixation of the knee joint in extension; refracture or reseparation also has been known to occur.

Prolonged disability is common as a result of the long fixation of the knee joint. For this reason many surgeons have returned to fixation by means of silver or bronze wire. The use of the massive fascial graft gives accurate approximation of fragments and allows immediate active motion of the knee joint. Whether or not real bony union takes place is uncertain, but the fragments do not separate with use, and owing to the safety of early motion of the joint, the disability is reduced to a minimum.

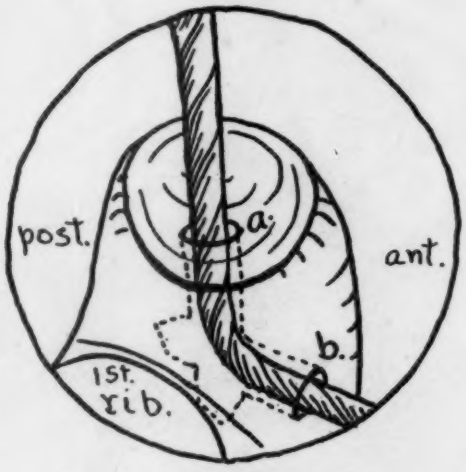

Fig. 4.—Lateral view illustrating method of drilling the sternum at an angle, avoiding danger of complete penetration from front to back.

Fig. 5.—A flexible silver probe, with eye, is the most suitable instrument found to follow the course of the drill holes through bone. Fascia in widths given in the text, when rolled, will follow without difficulty drills of correct sizes.

A 5 mm. drill is used and a strip of fascia lata 3 cm. wide and 24 cm. long is passed through. After careful approximation is obtained, one end is fenestrated. The portion of the graft penetrating the upper fragment is sutured to the prepatellar tendon with no. 1 chromic catgut sutures, while the portion passing through the lower fragment is carried upward and fixed to the quadriceps femoris in the same manner (figs. 6 and 7). Where the fascia overlaps itself, other inter-

rupted sutures of catgut are inserted. The rent in the lateral extension of the capsule is closed with interrupted no. 2 chromic catgut sutures. It is not necessary to use fascia for these sutures as the tear is through fascial structures which heal readily, once they are approximated, and there can be little, if any, strain on this region, owing to the absolute

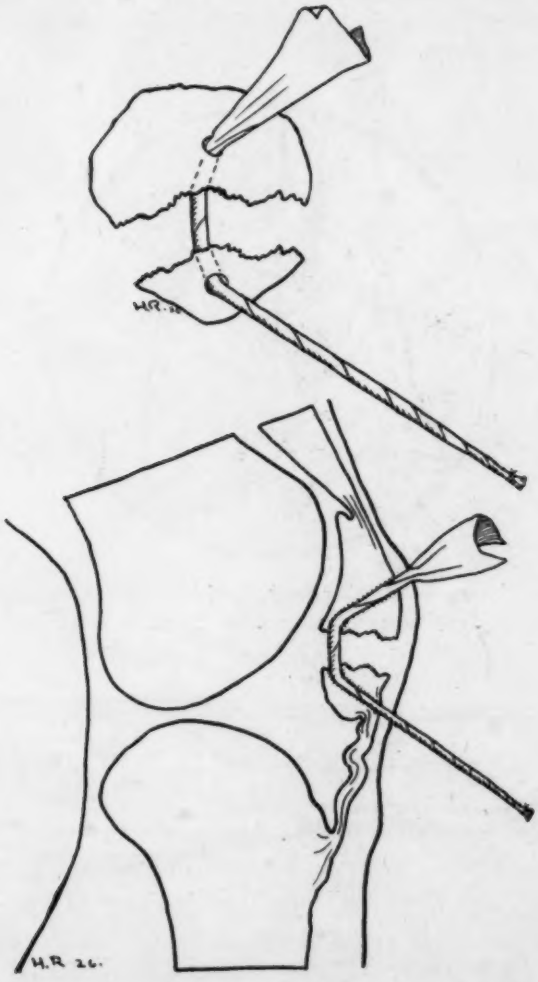

Fig. 6.—Method used in fracture of the patella. Note the oblique fenestrations in the fragments. The fascia is 3 cm. by 24 cm.; the drill, 5 mm.

fixation of the fragments of the patella with the fascial graft. Care should be used not to pentrate the joint surface of the patella with the drill. Although in many cases the lower fragment is found badly comminuted, there is usually one principal fragment which can be drilled

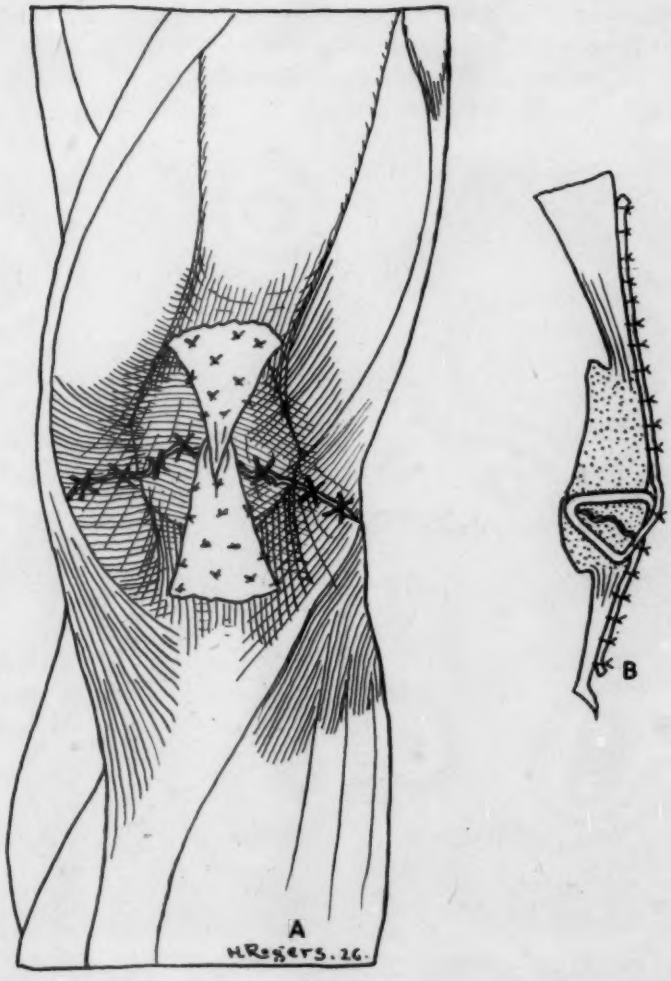

Fig. 7.—*A* illustrates complete fixation of fracture of the patella. The graft can rarely be too long, as the more of it is sutured to the quadriceps above, and to the prepatella tendon below, the stronger the fixation. Note the repair of the lateral extension tear with no. 2 chromic catgut. *B* is a lateral diagram of completed fixation. Note the lack of joint penetration.

successfully. If such comminution should exist that a fragment of suitable size cannot be found, the graft can be passed beneath the whole of the lower portion and brought out through the patellar tendon immediately below the bone. This has not been found necessary in any case as yet. The graft is taken from the uninjured thigh for several reasons; principally, because the long wound is prone to interfere with early active motion of the knee joint which is begun the day following operation. Also, it is often desirable to have the graft prepared by

Figure 8

Figure 9

Fig. 8.—Lateral view of fracture of the patella.

Fig. 9.—Fracture of the patella shown in the preceding figure shortly after fixation by massive fascial graft. Note the excellent approximation of fragments.

an assistant while the patellar fragments are being exposed and drilled Flexion of the knee beyond 90 degrees should be obtained in less than twelve weeks. Walking should be allowed at the end of four weeks, at first with crutches, weight bearing being gradually allowed to the point of discomfort. After ten weeks, aid should not be needed in walking.

FRACTURE OF THE OLECRANON

Open reduction of this fracture is becoming more popular following comparative studies of end-results. In cases in which gross separation of fragments has occurred, inability to obtain a satisfactory reduction and the long period of fixation in extension necessary to obtain union have brought about more radical measures. The time element of dysfunction has been longer than it should be in many of these cases, and some type of fixation should be used that allows early active

Fig. 10.—Same as figures 8 and 9 three months after fixation; the patient is now walking. There has not been any tendency for fragments to separate.

motion of the joint. Suture of the torn capsule with ordinary suture material gives good approximation of fragments, but motion must be delayed and reseparation of fragments may occur. Fixation with wire or pegs may allow early motion, but frequently necessitates a second operation for removal of the foreign body. Fixation by means of fascia lata is more nearly ideal than by these other methods. Three patients have been treated in this way so far. Wire had been used previously in the first case, the wire breaking, allowing reseparation at the end of

Fig. 11.—Patient whose roentgenograms are shown in figures 8, 9 and 10, showing amount of active flexion at the end of three months. Note the absence of scar from the thigh on this side. The fascia is taken from the opposite thigh.

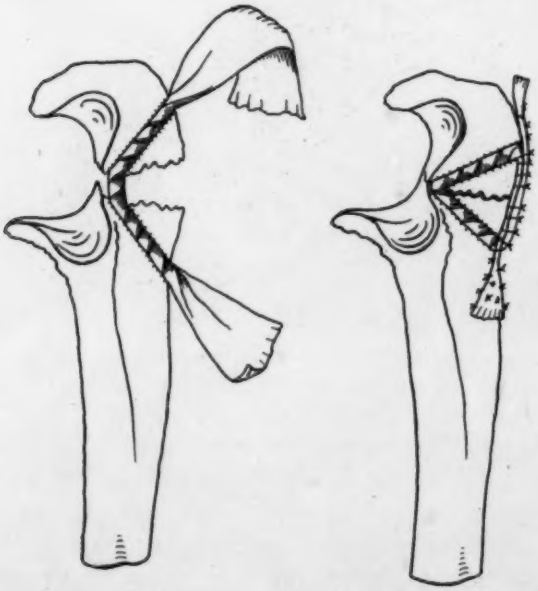

Fig. 12.—Method of fixation of fracture of the olecranon. Care is taken not to penetrate the joint with the drill. The graft is 2 cm. by 20 cm.; the drill, 3 mm. in diameter. The operation is completed as in figure 7 *A* of the patella.

ten weeks. The massive graft of fascia lata is used as in the patella. Here again care is taken to pass the drill obliquely so as to prevent penetration of the articular surface (fig. 12). A slightly curved incision is used through the soft parts in order to protect most of the graft from the superficial suture line. Motion is started almost immediately, with gratifying results as regards length of disability and complete restoration of function. A 3 mm. drill is used and a strip of fascia 2 cm. in width and 20 cm. in length is sutured to the triceps tendon and fascia above, and to the fascia of the forearm below with chromic catgut O sutures. The torn capsule is sutured with interrupted no. 1 chromic catgut.

Fig. 13.—Fracture of the olecranon. The tremendous swelling is due to primary treatment with straight splint applied with adhesive tape. The arm was suspended until the swelling subsided. Fascia lata fixation was performed two weeks after injury.

RECURRENT ANTERIOR SUBLUXATION OF THE RADIAL HEAD

A relaxation or a rupture of the orbicular ligament, sufficient to allow the radial head to luxate repeatedly, is an uncommon occurrence in our experience. The one case observed follows.

A thin, healthy, muscular American man, aged 21, while lifting the end of a heavy packing case felt a sudden snapping in his elbow. He was immediately disabled and in great pain with his arm extended, flexion at the elbow and rotation of the forearm being impossible. A physician was called who manipulated the arm without an anesthetic, during which a click was heard followed by

immediate comfort and restoration of motion. A sling was applied and within a few days the man returned to his work. A short time afterward, while producing the same strain, a recurrence of his disability took place. This time the patient and his fellow workmen managed the manipulation successfully, and the man kept at work, favoring his arm as much as possible. After a third recurrence, he applied for treatment.

On examination, the arms were identical in appearance. There was no swelling or discoloration. There was complete motion in all directions and he seemed to be able to hyperextend all his joints. There was no demonstrable tenderness. A roentgenogram failed to show any abnormality. As his disability had always resulted from lifting while his arm was extended, a plaster of paris cast was applied from the wrist to the axilla with elbow held at right angles. With this

Figure 14

Figure 15

Fig. 14.—Fracture of the olecranon shown in preceding figure, after fascial fixation.

Fig. 15.—Fracture of the olecranon, shown in two preceding figures, four weeks after fascial fixation, six weeks after injury.

the man continued at his work as best he could. The shell was removed at the end of six weeks, and aside from some muscular atrophy, the arm seemed to be normal. In a few days, however, he returned with the story that the condition had recurred during the night, awakening him from sleep. After considerable difficulty, he was able to restore the motion and regain comfort. At this time, ecchymosis or swelling about the elbow was not evident. There was normal motion in all directions. By reproducing the lifting strain, the man was able to demonstrate his lesion. There was a sudden fulness in the anterior cubital space, associated with a depression over the head of the radius on the lateral aspect of

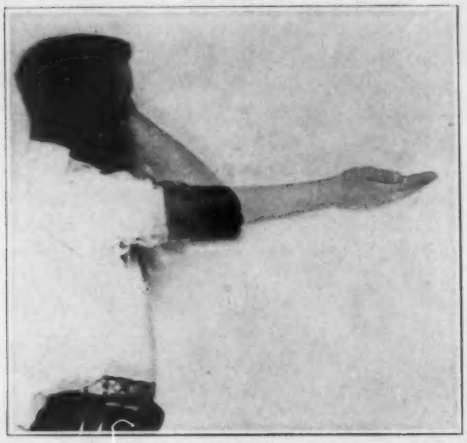

Fig. 16.—Photograph of patient whose roentgenograms are shown in figures 13, 14, and 15, taken four weeks after fascial suture of the olecranon. The superimposed exposures show the amount of flexion and extension of elbow. The patient was allowed to return to moderately heavy work six weeks after operation.

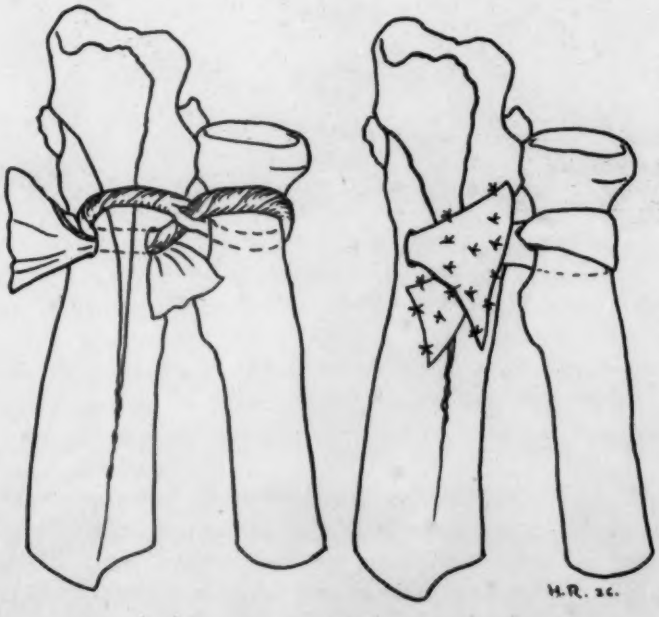

Fig. 17.—Schematic representation of method used in substituting a fascial graft for the orbicular ligament in the case of recurrent anterior dislocation of the radial head.

the joint. The arm was held in extension, and rotation of the forearm was impossible. By gentle traction on the forearm and flexion of the elbow the dislocation was easily reduced.

Operation was advised and accepted. Through a curved incision over the outer aspect of the elbow, the region of the head and neck of the radius and the triangular portion of the upper end of the ulna was exposed. After considerable difficulty, a strip of fascia lata 1.5 cm. wide and 15 cm. long was successfully passed around the neck of the radius. This was fenestrated and passed through a 3 mm. drill hole in the triangular portion of the ulna, and sutured to itself with several no. 0 chromic catgut stitches. Gentle motion was started at the end of forty-eight hours. Within four weeks, complete motion had returned, and

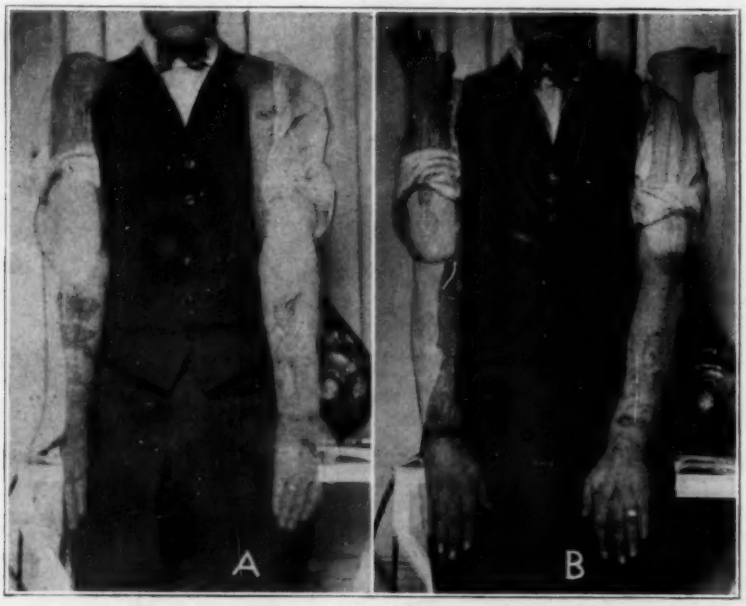

Fig. 18.—Superimposed exposures of the patient three months after operation for recurrent anterior dislocation of radial head. A complete range of motion is illustrated. *A* indicates the patient in supination; *B*, in pronation.

three months after the operation he was allowed to resume his work. The disability had not recurred a year after the operation.

SUMMARY

A method of using massive grafts of fresh, autogenous fascia lata in the repair of certain acute lesions of bones and joints is presented. The technic is simple and does not require any unusual apparatus. Fascia lata in the proposed widths and lengths will withstand as much strain on it as any of the foreign body materials in common use for such procedures. It has the distinct advantage of retaining life and forming a permanent structure.

CONTRACTION OF THE GALLBLADDER IN THE COMMON BULLHEAD (AMEIURUS NEBULOSIS) *

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It is now generally accepted by almost all who study the physiology of the gallbladder that it empties through the cystic duct. Furthermore, the conviction that it is emptied by the contraction of an intrinsic musculature is becoming more and more assured. Recent observations on the gallbladder of man (Levine [1]), as well as the observations of Ivy and Oldberg [2] on the effect of secretion on the gallbladder, further substantiate the conclusions of many others that the wall of the vesicle does contract and thereby expels bile into the cystic and common duct.

As would be expected, most of the recorded observations on the emptying of the gallbladder have been made on common laboratory mammals, such as the dog, cat, rabbit and guinea-pig, because of their accessibility and because of their higher phylogenetic position with an anatomic organization more closely allied to that of man. Relatively few observations have been made on birds, although I have considerable unpublished data on the contraction of the gallbladder in the hen and on the contraction of the common hepatic duct in the pigeon. The reptilians and amphibians remain unexplored as regards this particular process, although I have observed the gallbladders of a few turtles and frogs. Higgins and Mann (1926 [3]), in reporting studies of the gallbladders of dogs and guinea-pigs, recorded a few cursory observations on the biliary vesicle in the garpike *(Lepidosteus)*.

Generally, however, the lower vertebrates have contributed but few data to the wealth of information hitherto recorded on the functional activity of the extrahepatic biliary tract. Such a dearth of facts is in a measure lamentable, for in these phylogenetically older and less differentiated species fundamental physiologic processes maintain. It is a fact that with increased specialization and subsequent differentiation accompanying the development of higher forms, some modification

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* From the Division of Experimental Medicine and Pathology, The Mayo Foundation.

1. Levine, Samuel: Contraction of the Gallbladder Seen in Man, Arch. Int. Med. **40**:420 (Oct.) 1927.

2. Ivy, A. C., and Oldberg, Eric: Contraction and Evacuation of Gallbladder Caused by Highly Purified "Secretin" Preparation, Proc. Soc. Exper. Biol. & Med. **25**:113, 1927.

3. Higgins, G. M., and Mann, F. C.: Observations on the Emptying of the Gallbladder, Am. J. Physiol. **78**:339, 1926.

of the fundamental body processes may be expected. Nevertheless, a thorough understanding of the fundamental biologic principles that maintain in the lower vertebrates will facilitate the interpretation of the physiologic activities which regularly go on in the mammal.

With the foregoing in mind, a study of the biliary tracts of a large number of fresh-water fishes was undertaken. Through the courtesy of Mr. H. L. Canfield of the United States Bureau of Fisheries at La Crosse, Wis., the entire facilities of the numerous fisheries along the upper Mississippi river were placed at my disposal. With the assistance of the crews employed at the station, a few representative fishes of nearly all the species which inhabit this region were brought to the station laboratory for study. After a preliminary fast the fishes were fed a meal of fat; then, at varying intervals, observations were made on the gallbladder and the extrahepatic biliary tracts. In accordance with existing data on mammalian gallbladders, it was found that in nearly all fishes that were given the meal of fat, the biliary vesicle had emptied within the ensuing two or three hours, and that they were again distended with bile after from four to six hours. In studying as many different species as were available at the station, it appeared that the common bullhead *(Ameiurus nebulosus)*, because of the anatomic relations of the gallbladder, liver, common duct and duodenum, would lend itself most suitably to continued observation on the motor activity of the gallbladder and the common bile duct. Again through the courtesy of Mr. Canfield, several cans of these fishes were shipped to Rochester, where they were confined in laboratory tanks equipped with running water, and the following observations were made.

ANATOMY OF THE LIVER AND BILIARY TRACT

The liver of the common bullhead is slightly asymmetric and lies in the anterior third of the peritoneal cavity in close contact with the anterior surface to the septum transversum. Although the liver is a single organ, it is composed of two lobes of which the left is somewhat the larger. Each of these two possess smaller anterior, lateral and posterior lobes, thus giving to the margin of the entire organ a somewhat serrate appearance (figs. 1 and 2).

A short esophagus continues posteriorly from the pharynx along the dorsal surface of the liver and between the two main lobes. Slightly posterior to the hilum of the liver, the esophagus continues into a pear-shaped stomach which lies to the left of the median line, posterior and medial to the caudal prolongation of the left lobe of the liver. The stomach continues into the duodenum, which is shaped somewhat like a horseshoe, and makes a wide bend to the right passing through the hilum of the liver, and then posteriorly along the right side of the peritoneum.

Fig. 1.—The liver, gallbladder and gastro-intestinal tract of the common bullhead. The gallbladder is slightly elevated, and the lobes of the liver reflected.

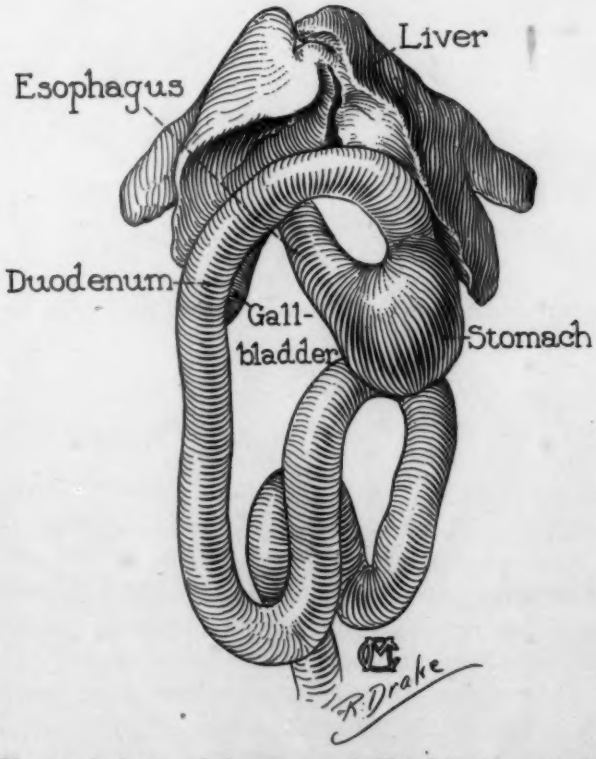

Fig. 2.—Liver and viscera of the common bullhead in the normal position.

The gallbladder and the extrahepatic biliary tract lie within the portal area, between the liver and the duodenum. The gallbladder lies on the right side of the peritoneal cavity, just dorsal to the descending limb of the duodenum and posterior to the right lobe of the liver, but relatively free from it. It is supported in position by the hepatoduodenal omentum through which several venous channels pass from the intestine by way of the gallbladder to the liver. From six to eight hepatic ducts of varying size empty into an elongated common duct which pursues an arcuate course along the inferior surface of the liver from the neck of the gallbladder to the dorsal surface of the duodenum, 12 mm. from the pylorus. A large hepatic duct, occasionally double, which drains the main portion of the right lobe of the liver,

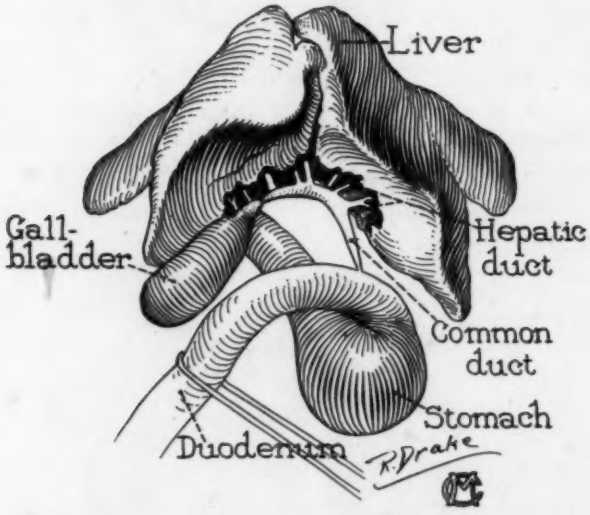

Fig. 3.—Partial dissection of the extrahepatic biliary tract in the common bullhead.

appears to empty directly into the neck of the gallbladder. The remaining portion of the liver is drained by a number of ducts which empty into the common duct (fig. 3). In the upper portion of the common duct, from about 3 to 5 mm. distal from the gallbladder, there is a restricted region which usually appears to be in a state of greater tonus than any other portion of the hepatic tract. From this point the dimensions of the common bile duct increase in both directions, and this portion of the hepatic system seems to bear some significant relationship to the physiologic responses that ensue on a fat meal. The common duct from the neck of the gallbladder to the duodenum, when in a state of rest, varies from 18 to 25 mm. in length among the different fishes examined. Its greatest diameter, about 2.5 mm., is near the

juncture of the left hepatic duct, from which point it gradually decreases until at the duodenum the duct is approximately 0.5 mm. in its cross dimension.

The venous drainage of the gastro-intestinal tract is unusually large for so small an animal (fig 4). The hepatic portal vein carries most of the venous blood from the intestine to the liver, but in addition, numerous smaller venous channels continue anteriorly from the horizontal and the descending portions of the duodenum to the liver.

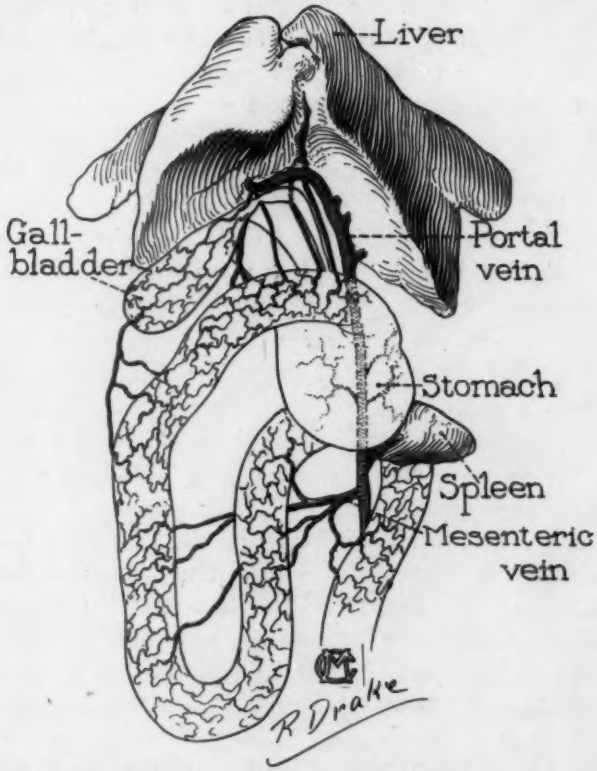

Fig. 4.—Venous drainage of the gastro-intestinal tract and the gallbladder in the common bullhead.

The hepatic portal vein, which lies on the right side of the peritoneal cavity, is formed by the channel carrying the blood from the posterior region of the body together with the large mesenteric vein which receives the blood from the colon, the small intestine and all but the anterior 50 mm. of the duodenum. After receiving a short but rather large splenic vein, the hepatic portal vein continues anteriorly along the dorsal surface of the fundus of the stomach, dorsal to the pylorus and into the area of the hilum of the left lobe of the liver. In its course it receives branches from the dorsal surface of the stomach, the esophagus

and the dorsal surface of the pylorus. The main channel then continues medially along the inferior surface of the left lobe of the liver and in its course gives off four main veins which enter the substance of the liver while its ultimate distribution is to the inferior surface of the right lobe of the liver where it bifurcates into two main channels which enter the right lobe near the neck of the gallbladder. The veins which drain the ventral wall of the stomach, the duodenum near the pylorus, and the common bile duct, all course independently forward to empty into the portal vein on the inferior surface of the left lobe of the liver. The remaining portion of the duodenum, however, down to within 50 mm. of the pylorus, is drained by from three to five independent veins which course obliquely forward into the region of the juncture of the gallbladder with the common bile duct and then empty into the portal circulation of this side. The venous distribution is unique in the sense that the radicles carrying the blood from the anterior 50 mm. of the duodenum do not have any relation with the hepatic portal system as such, but course independently forward and appear to be definitely associated with the venous drainage of the gallbladder.

With few exceptions, the foregoing description of the anatomic relations of the liver, the gastro-intestinal tract and the related blood supply is most commonly encountered. In this study of seventy-five fishes, however, one fish was opened in which there was complete reversal of the organs of the peritoneal cavity. The lobes of the liver were of the usual proportions, but the larger one was on the right side. Likewise, the pear-shaped stomach was on the right side and the duodenum made the usual broad curve from the pylorus on the right up through the hilum of the liver around to the left side of the peritoneum. The gallbladder was directly below this descending limb of the duodenum; it was slightly larger than the normal vesicle, but was joined to the usual extrahepatic biliary system, all of which was reversed.

THE EMPTYING OF THE GALLBLADDER

A phase of this study which is strikingly significant in the light of the present controversy on the emptying of the gallbladder is the contraction activity of the organ in response to a meal of fat. Since the gallbladder is free from the liver and may readily be exposed by simple traction on the duodenum, it is a simple procedure to open the fish, expose the vesicle and observe it for prolonged periods (fig. 5). Early in this study it became evident that the usual physiologic processes would go on only when the viscera so exposed were bathed in a physiologic solution of sodium chloride. Various solutions were tried including Ringer's and Tyrodes, but perhaps the more satisfactory results were attained by 0.6 per cent solution of sodium chloride in tap

water, the salt content of the latter being unusually high. It was necessary too, during these observations to devise means of properly aerating the fish. Although the bullhead is unusually hardy, it is sensitive to the loss of aeration, and consequently, many fishes were lost during the earlier investigations. Numerous methods were tried, but the one which was finally resorted to and which has proved satisfactory was the use of 0.6 per cent sodium chloride in tap water. This solution is oxygenated, passes by gravity through a two-way cock into a copper tank and into the mouth of the animal. The fluid bathes the gills and passes back over the viscera and then out of the tank through the second aperture. A constant stream of oxygenated solution passes over

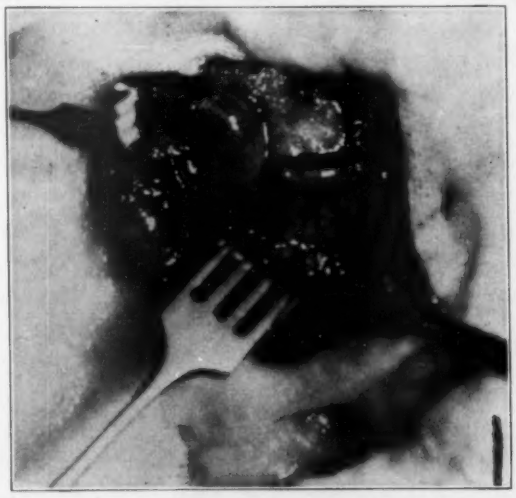

Fig. 5.—Exposed viscera, including the gallbladder, of a bullhead under observation.

the fish during the entire experiment, from two to three hours, thus meeting in every way the needs of the fish and of the experiment.

The fish to be studied is opened by a median abdominal incision extending 5 cm. posteriorly from a line joining the bases of the pectoral fins. The abdominal wall is then cut transversely for a distance along a line 15 mm. posterior to these fins, and the corners thereby formed are reflected and made fast to the tank. Slight bleeding occasionally ensues, but this is easily stopped and the animal remains quietly within the tank, with normal respiration in progress and the essential viscera exposed.

As in all of our observations on the emptying of the gallbladder in laboratory animals, egg-yolk and cream have been used. The fish is opened when the stomach and intestines are in a state of collapse, since food has not been ingested for some time. The gallbladder, however,

is well distended and the extrahepatic biliary tract is easily recognized. Two cubic centimeters of egg-yolk and cream is then injected directly into the duodenum, about 1 cm. from the pylorus. Immediately, peristalsis of the duodenum is set up. This may have its inception at the point of puncture, or, as often happens, complete contraction of the duodenum occurs at a level 40 mm. below the pylorus. From this point a wave continues posteriorly along the intestine; an antiperistaltic wave also usually passes backward to the pylorus. Active peristalsis and antiperistalsis then ensue. Many waves may arise at the pylorus, while others may arise at various distal points and travel in both directions for varying distances. Frequently, too, peristaltic waves are set up in the stomach. These arise in the region of the posterior fundus, and the entire stomach is literally crowded up against the pylorus. This is a reflex response on the part of the stomach, for during the peristaltic activity of the duodenum the pyloric sphincter has remained intact, and regurgitation into the stomach has not occurred, for the latter remains pale and flaccid while the duodenum is markedly colored by the injected fat.

During the rather extensive duodenal activity in which peristaltic waves have passed repeatedly over the orifice of the common bile duct, there has been no effect on the gallbladder. The entire extrahepatic biliary tract has remained inactive so far as any muscular movement is concerned, and it may be positively concluded that peristalsis does not have any inciting influence on the discharge of bile from the gallbladder.

As the injected fat is gradually forced posteriorly, peristalsis of the duodenum becomes less frequent. After thirty minutes an additional 2 cc. of egg-yolk and cream is given in the same way, and again the duodenum becomes active with waves of varying strength and duration. At the end of an hour 2 cc. more is given, so that 6 cc. of fat constitutes the test meal. As yet there is no indication that the gallbladder will become active, for it hangs just dorsal to the duodenum well distended with bile, its walls somewhat flaccid and without tone. The more or less forceful movements of the duodenum which is in contact with the ventral wall of the vesicle fail to induce movement within the gallbladder. Gradually, however, at intervals after giving the first 2 cc. of fat, ranging from an hour and fifteen minutes to an hour and forty-five minutes, an initial tonus is discernible over the entire surface of the gallbladder. There is no movement as yet, but the flaccidity is lost and the wall becomes tense and frequently somewhat lighter. At this time, too, there is slight evidence of contraction in the upper part of the common duct. If the overhanging lobes of the liver are now gently retracted so as to avoid mechanical irritation, marked constriction of the upper common bile duct, about 3 mm.

from the gallbladder, may be recognized. The constriction of this region of the duct together with the onset of tonus over the wall of the gallbladder are the first indications that muscular activity of the biliary tract is likely to follow soon.

Generally within fifteen minutes after the onset of tonus in the gallbladder, contraction waves are visible over the entire vesicle and the common bile duct as well. These waves appear to have their origin at the restricted region of the common bile duct about 3 mm. from the neck of the gallbladder. From this point of departure these waves pass over the common duct, completely forcing out the bile within the duct into the duodenum. Either coincident with this duct wave, or frequently just after it, a wave arising from the same region passes in the reverse direction over the gallbladder, forcing out a quantity of bile into the common bile duct. These waves, then, originate in the common duct and pass over the neck of the gallbladder to involve the fundus as well. Each wave need not be complete in the sense that it involves the entire vesicle; frequently it may fade out after traversing

Fig. 6.—A single contraction wave passing over the gallbladder following a meal of fat.

over a half or third of the gallbladder. The picture that now presents itself is perhaps more aptly illustrated by that of a toy balloon. If one were to draw this balloon through a small loop which represents the contraction wave, the appearance would be much like that in the gallbladder of the fish during motor activity (fig. 6). All the contraction waves, however, do not travel in the reverse direction. Frequently after the contractile mechanism has been set in motion, by factors as yet undetermined, independent waves of contraction may arise at almost any level on the gallbladder and travel in both directions. They frequently begin at the fundus and travel part way or entirely over the gallbladder, expelling more bile into the common duct. Furthermore, these contractions need not always involve the entire diameter of the vesicle at any one level, for occasionally the contractile area may be restricted to only a small portion of the wall, so that peculiar and much distorted figures of an otherwise oval gallbladder are occasionally seen during the motor activity. There does not appear

to be any definite synchronous activity between the motor mechanism of the common duct and that of the gallbladder. Successive contraction waves have been observed to pass over the common duct, unaccompanied by any visible contraction of the gallbladder. Then, too, contraction waves of variable extent may involve all or a part of the gallbladder without any visible motor activity of the common duct. However, in what have been thought to be thoroughly healthy and vigorous animals, both common duct and gallbladder become contractile at about the same time following the ingestion of fats and remain so for a considerable period.

The waves of contraction in both the gallbladder and the common duct do not follow each other in rapid succession. I have often tried to determine the time interval between these successive contractions, but the frequency varies in the same animal and in different animals, dependent no doubt on certain undetermined physiologic factors. Usually such contractions follow each other at from two-minute to four-minute intervals. Although the waves are not frequent, when they once appear, they traverse either the common duct or the gallbladder at a rate as rapid as the normal peristalsis of the duodenum. Throughout this period of motor activity of the common bile duct and the gallbladder, the duodenum, except for occasional peristaltic movements, has been inactive. Thus the movement of the biliary tract is independent of the activity of the duodenum, and the gallbladder empties without the so-called sucking of the contracting duodenum.

The gallbladder may empty itself completely; it has often been noted on opening an animal that it was entirely void of bile, appearing contracted to not more than 2 or 3 mm. in diameter and to 8 or 10 mm. in length. This degree of emptying was never experienced in animals under observation. Although small amounts of bile were ejected with each contraction wave, the gallbladder usually failed to contract to less than one third of its original size. Gradually the waves become more infrequent and finally cease entirely, although considerable bile may still remain within the gallbladder. The accountable factors in the cessation of the flow of bile are unknown. Fatigue or confinement may be a factor, and yet when the fish is taken from the tank it is still vigorous and given to the usual habits of jumping and splashing. These fishes do not withstand laboratory confinement in the same way or so satisfactorily as do those of the ganoid group. I have retained garpike in laboratory tanks for long periods, but the bullhead gradually loses vigor and becomes inactive even though aerated water and food are provided. This marked lassitude is reflected in the physiologic response of the biliary mechanism to the usual meal of fat. Fishes that have been retained in laboratory tanks for two weeks are less likely to show marked motor activity of the biliary tract following

a meal of fat than those observed immediately on their arrival at the laboratory. In certain fishes thus confined, I have failed to observe any response to the fat, while in others, contraction waves of the common duct were faintly visible, but only after a prolonged interval following the administration of the meal. Obviously, then, to secure the best results, only healthy, vigorous fishes should be used, and these soon after they reach the laboratory.

HISTOLOGY OF THE EXTRAHEPATIC BILIARY TRACT

The gallbladder is an extremely delicate organ, but, nevertheless, following proper stimulation, it possesses sufficient contractile tissue to eject bile. In the extended condition, the wall in the region of the fundus is slightly more than one fifteenth of a millimeter thick. The mucosa, which comprises a little less than one half of the entire thickness of the wall, is composed of characteristic columnar epithelium of tall narrow cells with nuclei in the base. Differential staining shows that the remainder of the wall is a composite structure of connective tissue and muscle fibers interspersed with abundant vascular channels. There appears to be considerable interlacing of the two tissues, but most of the muscle fibers are grouped into a compact layer coursing in the circular direction and supported on the sides by connective tissue fibrils. In the neck of the gallbladder, the muscle fibers are more loosely arranged, and here it is easy to identify a narrow band of longitudinal muscle fibers and diagonal fibers, as well as those running around the vesicle. The longitudinal fibers are interspersed with connective tissue fibers.

There is gradual reduction in the proportions of the tract passing from the gallbladder to the common bile duct, but the tissues of one continue imperceptibly into those of the other. Within the upper portion of the duct a conspicuous band of muscle fibers, both circular and longitudinal, lies just external to an equally prominent layer of connective tissue, which is separated from high columnar epithelium by a thin basement membrane.

Grossly, the hepatic ducts which drain the right lobe of the liver appear to empty into the neck of the gallbladder. This is not actually true, for they penetrate only the serosal and muscular tunics of the vesicle and then continue posteriorly within the connective tissue of the duct just external to the mucosa (fig. 7). In some cases these hepatic ducts extend for 2 mm. or more within the intramural portion of the cystic duct before emptying into its lumen. In this connection, it may be noted that the tissue of the hepatic ducts resembles the rest of the biliary tract, with especially prominent circular and longitudinal bands of muscle. When the wall of the cystic duct is penetrated, however, it is found that all muscle tissue of the hepatic duct discon-

tinues, so that within the intramural portion of the upper part of the common bile duct, the hepatic ducts consist of columnar epithelium only, supported by a wide band of connective tissue. There are numerous small hepatic ducts, and as many as four of these have been observed to enter the wall of the major duct and course independently into its lumen (fig. 7).

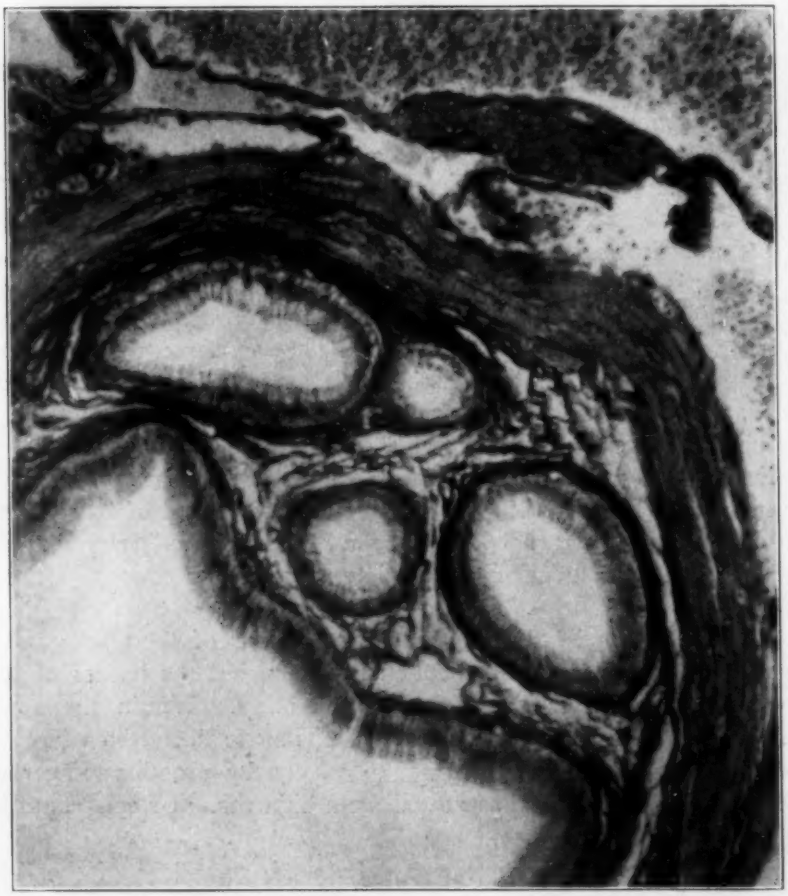

Fig. 7.—Partial cross-section of the neck of the gallbladder shows four hepatic ducts coursing within the connective tissue, between the mucosa and muscular tunics; × 220.

The anterior group of hepatic ducts which drain the right lobe of the liver empty into the lumen of the common duct within the region which is essentially active after the meal of fat. A constricted region of the upper part of the hepatic tract has been described from which as a center, contraction waves pass over the common duct and distally over the gallbladder. Sections of the tract at this point do not reveal

essential differences from the region immediately above or below; but a study of the distribution of nerves to this area, now in progress, may be instructive. The layer of muscle is more compact, however, and circular and longitudinal fibrils intermingle freely with a preponderance of the circular external to the longitudinal, but the layer of connective tissue immediately beneath the muscle is more loosely bound and more

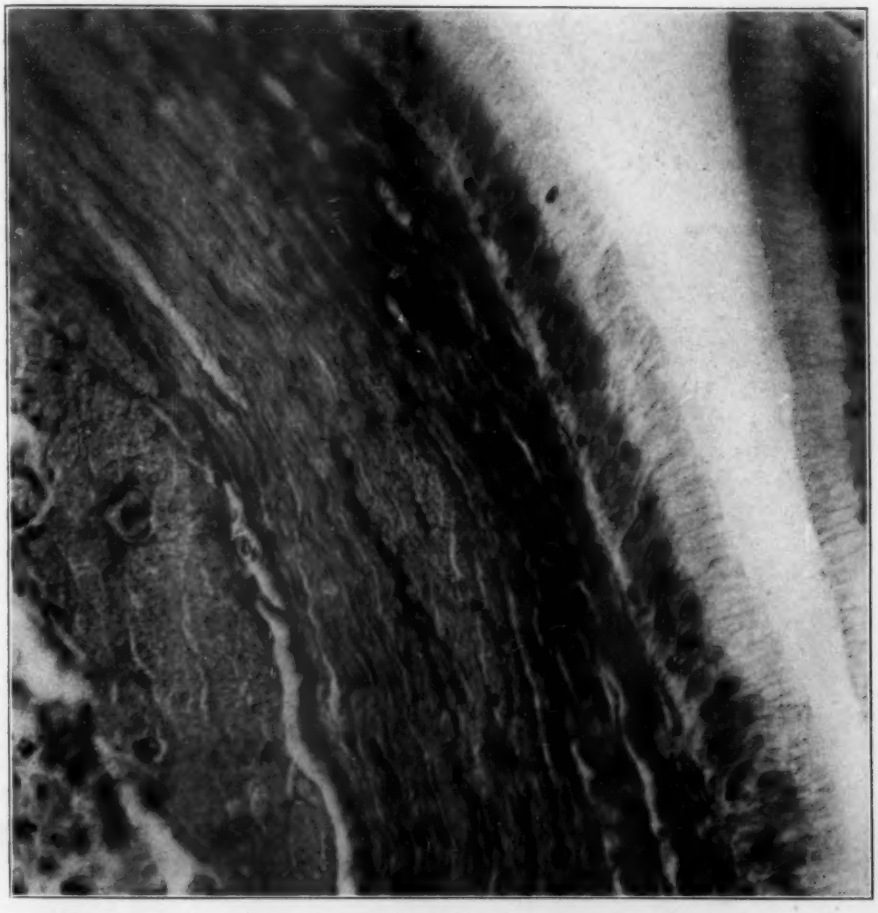

Fig. 8.—Partial cross-section of the wall of the common bile duct shows the wide band of muscle fibers external to the connective tissue layer; × 570.

hyperemic than elsewhere. The cells of the mucosa are more compressed than in other parts, a condition probably induced by the tonus of the muscle tunic at the time of fixation.

From this constricted portion of the hepatic tract, which perhaps could well be said to be the site of confluence of the neck of the gallbladder with the common duct, there is a gradual increase in the

diameter of the channel toward the duodenum. This increase reaches maximal proportions at the site of confluence with the hepatic ducts of the left lobe of the liver, from which point there is a gradual reduction in the circular dimensions of the common duct until it reaches the duodenum. This increase is largely due to an abundance of muscle fibers, both longitudinal and circular, which extend throughout the entire length of the common duct. In the upper portion of the common duct, the muscle and the layers of connective tissue are of equal width,

Fig. 9.—A cross-section of the intraduodenal portion of the common bile duct; wide band of muscle fibers and narrow zone of connective tissue may be noted; × 127.

while nearer the duodenum there is a progressive increase in the amount of muscle tissue and a decrease in the extent of the layer of connective tissue. In the lower part of the common duct, the layer of muscle is twice as thick as that of the connective tissue. Circular muscle fibers are more abundant but external to these, and in more or less restricted areas, there are scattered muscle bundles running longitudinally and diagonally (fig. 8). Continuing intraduodenally, the

preponderance of muscle tissue is even greater, and the connective tissue is restricted to a narrow zone immediately around the mucosa.

The bullhead differs from many higher vertebrates in that the common duct passes directly through the duodenal wall into the lumen of the intestine, opening by a single orifice. The muscle of the common duct continues throughout the entire intramural course, and there is an appreciable increase in the volume of this tissue within the duodenal wall. Whether this should be designated a sphincter of Oddi is questioned; it is but a continuation of the extensive musculature of the extraduodenal common duct and is not abruptly increased on entering the wall of the intestinal tract. A layer of muscle, however, entirely independent of the muscularis of the duodenum and approximately equal to it in thickness, surrounds the intramural portion of the common duct and is probably highly contractile during the evacuation of the biliary tract, such as occurs following the meal of fat (fig. 9).

COMMENT

These observations on the contraction of the extrahepatic biliary tract in the common bullhead following a meal rich in fats are interesting because of the facts disclosed pertinent to the manner in which the bile in the gallbladder is discharged. In studies hitherto reported, various conflicting interpretations of the mechanism of emptying the gallbladder have been advanced. Observations have been made on mammals, particularly on the cat and the dog, and anesthesia or extensive preliminary surgical procedures may have complicated the ensuing normal physiologic processes. These particular factors are probably obviated in the selection of the fish as a fit subject for such observations. It is not likely that the careful confinement of such an animal for any given length of time will essentially modify the physiologic responses of the body, nor is it likely that psychologic function would be so disturbed as seriously to impair the normal nervous activity accompanying the gastro-intestinal response to diet. Thus it would seem that in the fish one may observe the processes that obtain in a normal biliary tract uninterrupted or unmodified by the nervous reactions set up in more highly organized animals under essentially experimental conditions.

Obviously caution must be used in applying conclusions of observations made on a fish to the highly organized animal. It is probably true that in the modification of structure pursuant to specialization, differentiation in the physiologic response may have arisen; and yet with the present status and limitations of study one cannot be at all certain that contractile processes so clearly shown in the biliary tract of fishes may not be true for higher animals as well. The anatomic organization of the tracts in the various animals studied is essentially the same.

All observers agree that the biliary tracts of fishes and other animals are composed of serosa, muscle tunic of varying proportions, connective tissue sheath and mucosa of columnar epithelium. Differences may abound in the relative abundance of the various tissues involved or in peculiar modifications of certain of the tissues to form additional structures such as the valves of Heister, gland of Lushka or parietal sacculi, but the essential groundwork in the structural organization of these extrahepatic biliary tracts is identical. There is some basis for assuming, then, that there may be unity in the physiologic responses of these biliary tracts although phylogenetically so remote.

It is not my purpose here to attempt a correlation of fishes and other animals, or to attempt any explanation of the phenomena known to occur in the biliary tracts of mammals with facts observed in the fish. But rather, I wish further to substantiate certain conclusions hitherto reached from studies on the dog and the guinea-pig and to show that the lowly fish possesses an hepatic organization which responds to fat in a manner compatible with previously recorded data on the emptying of the gallbladder.

Gathered from the available sources of published data on the emptying of the gallbladder, various factors have been accorded some influence on the discharge of bile from the gallbladder. Chief among these are intra-abdominal pressure, secretory pressure of the liver, peristalsis of the duodenum together with duodenal tone and contraction of the muscle layer within the wall of the gallbladder. Certain of these factors have been stressed to the entire elimination of the others; but perhaps more recently the preponderance of data favors contraction.

In the light of recent observations, adequate data are presented to throw considerable doubt on the validity of certain of the foregoing factors. First, the animal under experiment is opened by a median abdominal incision so that a major portion of the viscera including the bile tract is exposed during the entire period. Extraneous pressure of any sort is thereby obviated, and the evidence points conclusively to the fact that intra-abdominal pressure or any other form of "squeeze" is not a factor in the discharge of bile from the gallbladder.

During the earlier part of the experiment, soon after the introduction of the fat in the duodenum, hepatic bile passes through the bile duct into the duodenum. This continues to flow for some time, and yet there is not the slightest evidence that the bile in the gallbladder is discharged into the common duct at any time during these early stages of the experiment.

When the abdominal cavity is opened, the entire gastro-intestinal tract is in a state of rest. The tract, being devoid of food for some time, is empty and the walls are collapsed. Immediately on the injection of 2 cc. of egg-yolk and cream into the duodenum, the tract comes

into tone, the muscles contract and peristalsis becomes active. Antiperistalsis of the duodenal region is especially characteristic. The stomach, although without the food as a stimulating factor, becomes contractile. These peristaltic waves of varying lengths and force which pass repeatedly over the orifice of the common bile duct do not appear to have any effect on the flow of bile. The gallbladder remains entirely inactive throughout the entire period that the duodenum is motile. The common duct, too, is inactive so far as movement is concerned during this interval. The conclusion is obvious, then, that peristalsis or muscle tone of the duodenum does not have any effect on the discharge of bile in this animal.

This entire study adequately supports the observation, now generally accepted, that bile is discharged from the gallbladder by the active contraction of an intrinsic musculature. The common duct is also shown to be contractile, aiding thereby the evacuation of the gallbladder. Extrahepatic biliary motility is not apparent until from an hour to an hour and a half after the injection of fat into the duodenum. This motility expresses itself in the form of contraction waves that arise in the upper part of the hepatic tract and travel toward the duodenum in one direction and back over the gallbladder in the other direction. These waves are not interrelated, for one may arise without the other. Usually a wave that arises at the customary site, to course toward the duodenum will pass throughout the common duct, while waves passing over the gallbladder are frequently incomplete. While the gallbladder is in a state of contraction, waves may arise at the fundus and pass partially or completely over it, as well as in the reverse direction.

The time interval before the contraction of the gallbladder following the introduction of the fat suggests that the causal factors involved in this motility are in some way related to absorption. The independent vascular connection of the duodenum with the gallbladder and the cystic duct is suggestive, and studies are now under way to determine, if possible, the absorptive route and the factors underlying the contraction of these biliary channels.

SUMMARY

The gross and microscopic anatomy and the motor activity of the extrahepatic biliary tract in the common bullhead are reported. In this animal, the gallbladder hangs relatively free from the liver and may readily be exposed by slight traction on the duodenum, so that continuous observations on the emptying of the gallbladder in response to a meal of fat are readily made. A method is described for properly aerating the animal and exposing the viscera preparatory to such continuous observation.

Following the intraduodenal injection of a few cubic centimeters of egg-yolk and cream, active peristalsis and antiperistalsis of the gastro-intestinal tract are induced. Hepatic bile is discharged into the duodenum, but the gallbladder remains inactive during the period of gastro-intestinal activity.

Within periods of time varying from an hour and fifteen minutes to an hour and forty-five minutes, muscle tonus over the gallbladder is apparent. Contraction waves soon pass over the vesicle and force out portions of the contained bile into the common bile duct. These waves originate within the upper portion of the bile duct near its continuity with the gallbladder and pass in a reverse direction over it. Likewise, contraction waves pass over the entire common bile duct and force the contained bile into the duodenum. Subsequently, contraction waves arise at the fundus of the gallbladder and pass over the vesicle to the bile duct. Waves of the common duct and waves of the gallbladder tunic are not necessarily synchronous.

There is conclusive evidence that: (1) the gallbladder in the common bullhead empties by the contraction of the muscle tunic within its wall; (2) the emptying of the gallbladder is related to the extent of gastro-intestinal absorption of fat; (3) intra-abdominal pressure is not a factor in the discharge of bile from the gallbladder, and (4) duodenal peristalsis or duodenal muscle tone is entirely ineffectual in the in the discharge of bile from the gallbladder.

PYOGENIC ARTHRITIS IN THE KNEE JOINT OF RABBITS

TREATMENT WITH GENTIAN VIOLET: EXPERIMENTAL STUDY *

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One of the frequently discussed problems of the present day is the use of gentian violet and mercurochrome in the treatment of disease and infection. The type of infection treated has not been limited to one group of cases. The exact nature of the reaction of these drugs in combating infection has not been satisfactorily explained. With this thought in mind, a study has been made of the reaction of gentian violet in joints infected with *Staphylococcus aureus*. This study has involved a careful investigation of this type of arthritis, and it is hoped that some light may be thrown on arthritis in general.

Churchman has published three articles on the treatment of infections of the joint with gentian violet. First, in 1915, he [1] demonstrated an apparatus for the irrigation of a joint, followed by an instillation of gentian violet. He felt that in joints with a purulent infection the synovial membrane should be cleared of the film of pus and necrotic tissue present before the instillation of the gentian violet. The gentian violet in a 1 to 10,000 solution could then penetrate the synovial membrane to destroy the organisms. In 1918, he [2] reported the perfected apparatus for joint lavage, and eight cases, in two of which successful results were obtained in pyogenic joints. In 1921, he [3] reported six cases, in two of which good results were obtained in staphylococcus infections. In 1924, Churchman [4] stated that the most striking characteristic of gentian violet was its bacteriostatic power, in addition to its bactericidal power. Its great value lay in its penetration into tissues, which is impossible for antiseptics not in the triphenyl methane group of dyes. He showed that in a human knee the dye stained the nucleus and protoplasm of the endothelial cells and penetrated to the underlying connective tissue, but did not injure the synovial membrane. He showed this in an infected joint treated first with lavage.

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* From the Louise Bowles Foundation of the Children's Hospital School, Baltimore.

1. Churchman, J. W.: Ann. Surg. **62**:409, 1915.
2. Churchman, J. W.: Treatment of Acute Infections of Joint, J. A. M. A. **70**:1047 (April 13) 1918.
3. Churchman, J. W.: Gentian Violet in Treatment of Purulent Arthritis, J. A. M. A. **75**:583 (Aug. 28) 1921.
4. Churchman, J. W.: J. Urol. **11**:1, 1924.

Cotton [5] recently reported five cases of pyogenic joints, in three of which there were infections with *Staphylococcus aureus*. He irrigated these with 1 to 15,000 mercuric chloride in salt solution, and the joints became normal. He said that so long as infection was confined to the synovial cavity, the joint was sterilizable. The question arises as to whether the mechanical cleansing is not the main factor in this treatment.

In 1925, Gatch, Trusler and Owen,[6] experimenting with intravenous injections into rabbits, showed that of a number of preparations of gentian violet the least toxic was physiologic sodium chloride solution. It was also shown that gentian violet in isotonic 4 per cent dextrose possessed less toxicity than gentian violet in distilled water. Gentian violet had a solubility of 39 per cent in physiologic sodium chloride solution compared to 94 per cent in distilled water. They concluded that gentian violet would exert a temporary bacteriostatic action in septicemia, but that the ultimate benefits depended on the resistive powers of the patient.

In 1925, Brill and Myers [7] showed that a blood medium made up with gentian violet to a dilution of 1 to 10,000 would kill the growth of a *Staphylococcus albus* organism only after twenty-four hours' contact.

In reviewing the literature on experimental arthritis, no reference can be found to joints infected with staphylococcus. All the experimentation has been with strains of streptococcus, mostly of the viridans type. A most interesting and instructive piece of work was done by Jackson [8] in 1913. Rabbits were given intravenous injections of a culture of streptococcus, and studies were made of the joints in from two hours to four months after infection. It was shown that after two hours the streptococcus could be demonstrated in the vessels of the periarticular tissues. In ten hours intravascular collections of leukocytes were present. In twenty-four hours there was an exudation and and migration of the leukocytes into the joint cavity. Thus, there was an incubation period of twenty-four hours between the time of the intravenous injection of the streptococcus and the time the joint becomes infected. The changes were only those consistent with the varying phases of a single inflammatory process. The changes depended on the independent localization of the bacteria in the joint cavity, in the tissues

5. Cotton, F. J.: J. Bone & Joint Surg. **8**:395, 1926.

6. Gatch, W. D.; Trusler, H. M., and Owen, J. E.: Treatment of General Septicemia by Gentian Violet and Mercurochrome-220 Soluble, J. A. M. A. **85**: 894 (Sept. 19) 1925.

7. Brill, I. C., and Myers, H. B.: Mercurochrome-220 Soluble and Gentian Violet, Bactericidal Efficiency by Intravenous Route, J. A. M. A. **84**:879 (March 21) 1925.

8. Jackson, Leila: J. Infect. Dis. **12**:364, 1913.

surrounding the blood vessels of the synovial membrane, in the plica synovialis, in the tendon sheaths and in the blood vessels of the periosteum and bone marrow near the epiphyseal cartilage. The involvement of the perisynovial and parasynovial structures was marked, and some nodular formation was found in the tissues about the joint.

In 1915, Faber [9] showed that by a process of first injecting small quantities of a culture of a strain of *Streptococcus viridans* into the joint, and of following this with one intravenous injection, arthritis could be caused constantly. Without previous sensitization of the joint, two or three intravenous injections were required to cause the arthritis.

In 1914, Rothschild and Thalhimer [10] showed that after intravenous injections of a *Streptococcus mitis,* arthritis was caused in 50 per cent of the rabbits experimented with, and that the organism could be recovered from one third of the affected joints.

OUTLINE OF EXPERIMENTS

First, the knee joint of the rabbit was directly infected by an instillation of 0.1 cc. of a twenty-four hour broth culture of a pure strain of *Staphylococcus aureus.* Second, when a definite local reaction was present in the knee, manifested by increase in local heat, swelling and limitation of motion, the joint was aspirated for culture and gentian violet was injected. The clinical manifestations in the joint were followed until the active process had subsided. During this period roentgenograms were taken. Frequent aspirations of the joint for culture were made. The animal was then killed, and the joint studied grossly and microscopically. From one to three injections of gentian violet of 1 cc. each were made following the infection. The gentian violet was used in strengths of 1 to 400 (0.25 per cent) and 1 to 200 (0.5 per cent). It was prepared in three different mediums, namely, distilled water, 4 per cent dextrose and olive oil.

Thirty rabbits were used in the problem. Attempts were made to sterilize the infected knee joints of 20 of these. This was successful in seventeen, or 85 per cent of the cases. Four rabbits were used as *Staphylococcus aureus* controls, and three as gentian violet controls. Three rabbits died of intercurrent causes soon after the onset of the infection, one from an infection of the blood stream, one from a severe diarrhea following the instillation of the gentian and one from an unknown cause.

The report of the experimental work is divided into four parts, namely bacteriologic, clinical, roentgenologic and pathologic.

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9. Faber, H. K.: J. Exper. Med. **22**:615, 1915.

10. Rothschild and Thalhimer: J. Exper. Med. **19**:444, 1914.

BACTERIOLOGIC STUDY

A study was made of twenty-four infected joints. Seventeen were successfully sterilized, three were unsuccessfully sterilized and four were controls.

1. *Successfully Sterilized.*—These joints required from one to fifty-three days for the sterilization. The time depended on the frequency of administration, the strength and the medium of the gentian violet. They are divided into four groups, according to the gentian violet preparation used.

(*a*) 0.25 Per Cent Aqueous Gentian: Four rabbits were given from two to three injections in from one to twenty-one days after infection. The joints were sterile in from nineteen to fifty-three days, the average being twenty-one days. Two rabbits which did not show bacteriologic evidence of infection, but did show clinical evidence, were given one injection each. These showed a complete subsidence of the acute condition of the joints in a few days' time.

(*b*) 0.25 Per Cent Dextrose Gentian: Three rabbits were given from one to two injections in from one to three days after infection. The joints were sterile in from four to twenty-eight days, the average being thirteen days.

(*c*) 0.5 Per Cent Dextrose Gentian: Four rabbits were given from two to three injections in from one to three days after infection. The joints were sterile in from two to four days, the average being three days.

(*d*) 0.5 Per Cent Olive Oil Gentian: Four rabbits were given three injections in from one to four days after infection. The joints were sterile in from fifteen to twenty-nine days, the average being twenty-two days.

2. *Unsuccessfully Sterilized.*—One animal received two injections of 0.25 per cent aqueous gentian in two and four days after infection. Two received two injections each of 0.25 per cent dextrose gentian in from one to five days after infection. One of the latter two showed a negative culture at the end of ten days, but later on the twenty-eighth and thirty-second day positive cultures were obtained.

3. *Control Staphylococcus aureus.*—The four rabbits in this group showed positive cultures. One of these, however, had a negative culture on the twenty-eighth day, but later on the forty-second day at autopsy the culture was positive.

CLINICAL STUDY

The most important clinical evidence of infection noted were the limitation of motion, the swelling and the increase in local heat. The first two signs were the most exact and had the most relative value in the making of a comparison of the amount of clinical activity in the joints. The limitation of motion is reported in degrees of limitation of extension; for instance, a joint capable of extension only to a right angle is reported as 90 degree' limitation of extension. The limitation of motion is placed in the following four groups: (1) between 0 and 10 degrees; (2) between 10 and 60 degrees; (3) between 60 and 90 degrees, and (4) between 90 and 135 degrees. The amount of swelling is reported as slight, fair, moderate or large. The last examination of the knee in the living animal is used in the analysis, as shown

in table 1. All the joints of the successfully sterilized, the unsuccessfully sterilized and the control groups are listed according to the amount of motion and swelling, with an average of each group. In figure 1, there is a comparison of the amount of motion in each group over a period of thirty days. In figure 2, there is a comparison of the amount of motion in each of the four gentian groups of the sterilized joints over a period of thirty days.

ROENTGENOLOGIC STUDY

In taking the roentgenograms attempts were made to follow the clinical changes of the joints in the different stages of activity. From

TABLE 1.—*Degree of Clinical Activity in All Joints Manifested by Limitation of Motion and Swelling*

Limit of motion / Swelling	0	1°–10° Slight	10°–60° Fair	60°–90° Moderate	90°–135° Large	Average	Total Joints
1. Successfully sterilized							
(*a*) 0.25% aqueous gentian	..	..	..	..	..	..	6
(1) Limit of motion	..	1	..	2	3	87°	
(2) Swelling	..	1	3	1	1	Fair +	
(*b*) 0.25% dextrose gentian	..	..	..	..	..	..	3
(1) Limit of motion	..	1	..	..	2	85°	
(2) Swelling	..	1	1	..	1	Fair +	
(*c*) 0.5% dextrose gentian	..	..	..	..	..	..	4
(1) Limit of motion	..	1	..	3	..	57°	
(2) Swelling	..	3	..	1	..	Slight +	
(*d*) 0.5% olive oil gentian	..	..	..	..	..	..	4
(1) Limit of motion	..	..	..	2	2	87°	
(2) Swelling	..	..	..	4	..	Fair +	
2. Unsuccessfully sterilized	..	..	..	..	..	..	3
(1) Limit of motion	..	..	..	..	3	137°	
(2) Swelling	..	..	..	1	2	Moderate +	
3. Control							
(*a*) Staphylococcus aureus	..	..	..	..	..	..	4
(1) Limit of motion	..	..	..	..	4	117°	
(2) Swelling	..	..	..	4	..	Moderate	
(*b*) Gentian violet	..	..	..	..	..	..	3
(1) Limit of motion	1	2	..	..	..	7°	
(2) Swelling	3	..	..	..	..	—	
							27

one to five roentgenograms were made of every joint after the infection. Only the final roentgenogram in each joint is described here.

1. *Successfully Sterilized.*—(*a*) and (*b*) 0.25 Per Cent Aqueous and 0.25 Per Cent Dextrose Gentian: One animal showed a slight clouding, one showed irregular joint surfaces, two showed destruction of the bone on the opposing surfaces of the tibia, femur and patella and five showed all of the foregoing changes, in addition to changes in the tibia and femur proper, such as thinning of the lower end of the femur and thickening of the upper end of the tibia.

(*c*) 0.5 Per Cent Dextrose Gentian: A slight clouding of the joint spaces was seen without changes in the bone.

(*d*) 0.5 Per Cent Olive Oil Gentian: One animal showed irregular changes in the bone on the joint surfaces, and three showed changes in the lower end of the femur and upper end of the tibia.

2. *Unsuccessfully Sterilized.*—All these animals showed a large amount of bone destruction on the joint surfaces, and changes in the tibia and femur proper.

3. *Controls.*—(*a*) *Staphylococcus aureus:* All showed essentially the same changes as in the unsuccessfully sterilized group.

(*b*) Gentian Violet: No changes were noted in the joint surfaces or spaces.

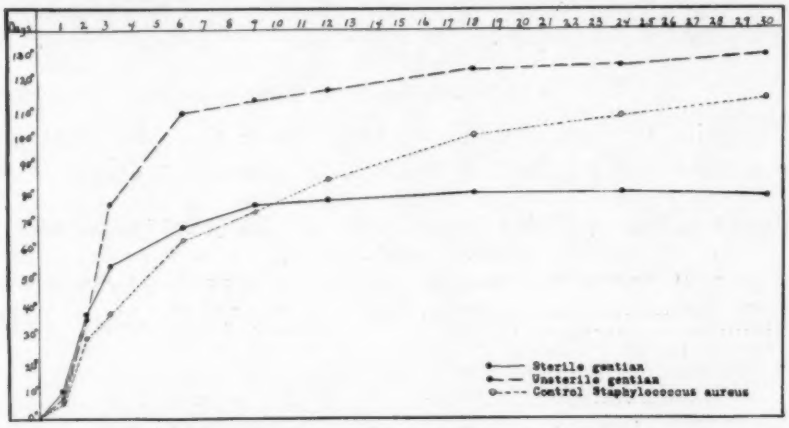

Fig. 1.—Clinical reaction in degrees of limitation of extension of the successfully sterilized, the unsuccessfully sterilized and the control joints infected with *Staphylococcus aureus* over a period of thirty days.

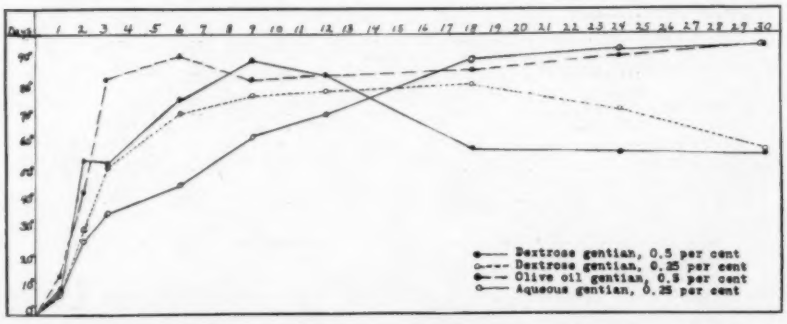

Fig. 2.—Clinical reaction in degrees of limitation of extension of the successfully sterilized joints in the group in which 0.5 per cent dextrose, 0.25 per cent dextrose, 0.5 per cent olive oil and 0.25 per cent aqueous gentian were used over a period of thirty days. The reaction was markedly less in the groups in which dextrose and gentian were used.

GROSS PATHOLOGIC STUDY

Eighteen of the twenty-seven joints were examined and the appearance of the joint structures was noted.

1. *Successfully Sterilized.*—(*a*) and (*b*) 0.25 Per Cent Aqueous and Dextrose Gentian: Seven of the nine joints in these groups were opened. Four showed a marked bone destruction of the surfaces of the femur, tibia and patella. Three

showed a severe fibrous tissue reaction in the joint proper. In six, nodules of cheesy, caseous material were seen about the joints. Pus was found in the joints of three, gentian in the joints of two and gentian in the surrounding tissues of five.

(*c*) 0.5 Per Cent Dextrose Gentian: Two of the four in this group were examined. One showed a rather large amount of gentian in the joint proper and in the surrounding tissues, without changes in the joint or pus. This was

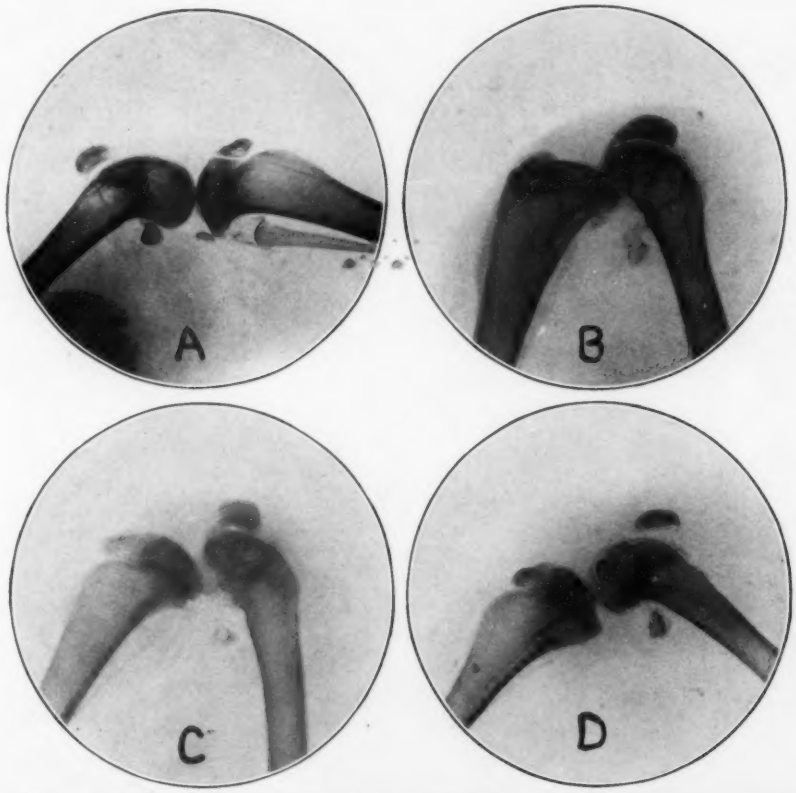

Fig. 3.—Early roentgen-ray changes in a successfully sterilized, an unsuccessfully sterilized and a control joint infected with *Staphylococcus aureus*. *A* indicates a normal joint; *B*, sterile joint of rabbit 28 on ninth day—0.5 per cent dextrose gentian injected; *C*, unsterile joint of rabbit 23 on eighth day—0.25 per cent dextrose gentian injected; *D*, control joint of rabbit 1 infected with *Staphylococcus aureus* on tenth day. The following points should be noted: (1) the clouding of joints *B*, *C* and *D*, compared with the normal joint *A*, and (2) the irregularity along the under surface of the patella, the anterior border of the femur and the posterior portion of the tibia in the control joint *D*, which is not seen in *B* and *C*.

on the twenty-first day after infection. The other joint was opened five and one-half months after infection. It presented an entirely different picture. There was a marked erosion of all cartilage with bits of cartilage in the joint. The

crucial ligaments were relaxed, and they allowed an abnormal amount of lateral mobility. A slight fibrous tissue proliferation was present on the sides of the joint.

(*d*) 0.5 Per Cent Olive Oil Gentian: Two of the four joints in this group were opened. These showed pus in the joint, and pus and gentian in the surrounding tissues. There was a roughening of the articular cartilage in both, with a thinning of the crucial ligaments and semilunar cartilages in one. The lower end of the femur in one showed a nodular swelling.

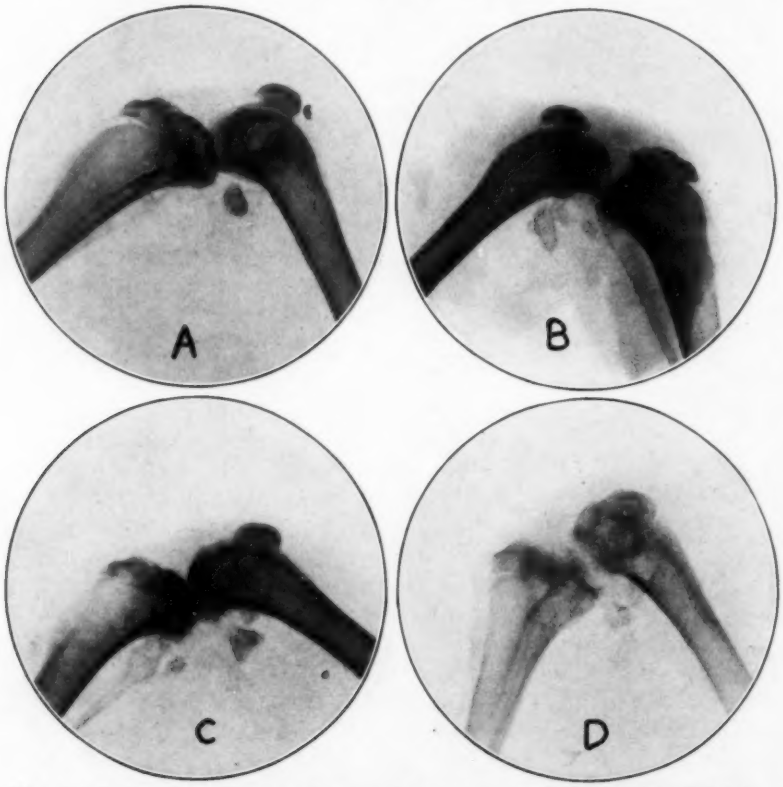

Fig. 4.—Later roentgen-ray changes in two successfully sterilized joints and one unsuccessfully sterilized joint, compared with a control joint in which gentian was used. *A* indicates a control joint, injected with gentian, from rabbit 15 on the thirty-second day—0.25 per cent dextrose injected; *B*, sterile joint from rabbit 26 on twenty-seventh day—0.5 per cent olive oil gentian injected; *C*, sterile joint of rabbit 21 on thirty-second day—0.25 per cent dextrose gentian injected; *D*, unsterile joint of rabbit 14 on thirty-second day—0.25 per cent dextrose gentian injected. The following points should be noted: (1) the complete absence of changes in the control joint *A*, in which gentian was used; (2) the marked irregularity and bone destruction in *B*, *C* and *D*, and (3) the areas of absorption in *D*.

2. *Unsuccessfully Sterilized.*—One of the three in this group was opened. This showed pus in the joint and tissues, gentian in the tissues, a marked fibrous tissue proliferation in the joint and a roughening of all bony surfaces.

3. *Controls.*—(*a*) *Staphylococcus aureus:* Three of the four joints in this group were opened. Two showed pus in the joint, a large fibrous tissue reaction in the joint and a roughening of all bony surfaces. One was opened seven months after the infection. This showed a large amount of fibrous tissue in the joint with evidence of new bone formation. All the cartilage had been destroyed. Frank pus was not encountered.

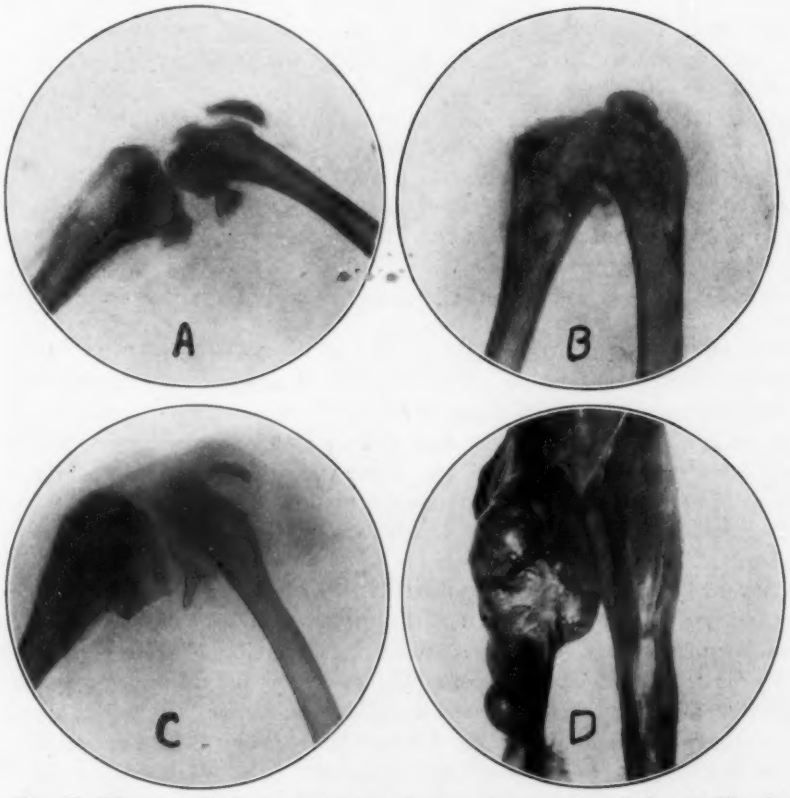

Fig. 5.—Most marked roentgen-ray changes in a successfully sterilized, an unsuccessfully sterilized and a control joint infected with *Staphylococcus aureus;* and the extra-articular caseous nodules found in many of the infected joints. *A* indicates a sterile joint of rabbit 5 on the eighty-sixth day—0.25 per cent aqueous gentian injected; *B,* unsterile joint of rabbit 10 on seventy-sixth day—0.25 per cent aqueous gentian injected; *C,* control joint of rabbit 1 infected with *Staphylococcus aureus,* on thirty-seventh day; *D,* extra-articular caseous nodules in rabbit 1 on thirty-seventh day. The following points should be noted: (1) the clouding, irregularity and bone destruction in *A, B* and *C;* (2) the areas of absorption in *B,* and (3) the thinning of the lower end of the femur and thickening of the upper end of the tibia in *C.*

(*b*) Gentian Violet: These three were opened and found to have a small amount of gentian in the surrounding tissues. Changes had not occurred in the joints.

MICROSCOPIC PATHOLOGIC STUDY

The data for the microscopic pathologic study is based on the sections of nineteen out of the twenty-seven joints. Only the general results will be given.

1. *Successfully Sterilized.*—(*a*) and (*b*) 0.25 Per cent Aqueous and Dextrose Gentian: Six of the nine joints were studied. Pus was found in the joints of five and in the tissues of three. In one there were three abscesses in the epiphysis of the tibia. The cartilage was eroded on the surface of the tibia in all and on the femur in all except one. In one the cartilage was found in the joint. In one, the cartilage showed a proliferation, while in another one the fibrous tissue was replacing the cartilage. There was a moderate fibrous tissue reaction in the joints of four. In one there was a definite increase of the fibrous tissue in the popliteal space. In four the bone marrow in the epiphysis was supplanted by fibrous tissue. In one there was a heavy fibrous band across the joint. The crucial ligaments and patella were normal in two. In one spicules of bone were present in the joint, with bony projections into the joint not covered by cartilage or fibrous tissue. Gentian was found in the joint of one and in the surrounding tissues of three.

(*c*) 0.5 Per Cent Dextrose Gentian: One of the four was studied. This was five and one-half months after the infection. Pus was found in the tissues. There was an erosion of cartilage on all the joint surfaces with sequestration into the joint. Parts of the joint showed bony spicules projecting into the joint space, completely denuded of cartilage. There was evidence of cartilage proliferation. A large amount of fibrous tissue was present in the joint with an increase in the popliteal space. The crucial ligaments were thinned. The reaction showed healing.

(*d*) 0.5 Per Cent Olive Oil Gentian: All four joints were studied. The joint reaction was more marked here than in any other group. Pus was present in the joints of three and in the surrounding tissues of one. There was an abscess in the femur of one. The cartilage of both the femur and tibia was eroded in all four with a sequestration of small bits into the joint. In one spicules of bone were present in the joint. In two the cartilage on the anterior surface of the femur was not eroded. A marked fibrous tissue proliferation was seen in all. In three fibrous tissue replaced cartilage, while in all four the bone marrow of the epiphyses was replaced with fibrous tissue. The posterior part of the capsule and crucial ligaments were thicker than normal in one.

2. *Unsuccessully Sterilized.*—Two of the three were studied. A large amount of pus was found in the joints and tissues. Abscesses were present in the bone, one showing the femur and tibia involved, and the other, only the tibia. One showed a large collection of pus beneath the periosteum on the anterior border of both the femur and the tibia. The cartilage was eroded over all the joint surfaces, and had sequestrated into the joint. A marked fibrous tissue proliferation was present through the joints. In one cartilage was replaced by fibrous tissue, while in another the bone marrow was supplanted by fibrous tissue.

3. *Controls.*—(*a*) *Staphylococcus aureus:* Three of the four were studied. One of these showed only a moderate reaction while the other two showed the most marked reaction in the series. The first showed a slight amount of pus and

erosion of cartilage, while the only evidence of fibrous reaction was a band across the joint. The latter two showed a large amount of pus in the joints with a slight amount in the tissues. Two large abscesses were seen in the tibia of one. There was marked cartilage erosion with sequestration into the joint. One showed spicules of bone in the joint. The fibrous tissue in the joint was marked. In one a heavy fibrous band ran across the joint. In both bone marrow was replaced with fibrous tissue.

(*b*). Gentian Violet: Little reaction was noted in the three. All showed an infiltration of leukocytes into the joint, and two showed a small amount of gentian. In the surrounding tissues of one gentian was found, and in another, an infiltration of leukocytes.

In summarizing the microscopic pathology four groups of changes have been noted:

(1) Acute inflammatory changes, such as pus and necrotic tissue in the joint and in the periarticular tissues; abscess formation around the joint, in the joint and in the bone proper, and pus beneath the periosteum of the bone.

(2) Cartilaginous changes, such as erosion, destruction and sequestration into the joint, and proliferation.

(3) Bony changes, such as spicules of bone projecting into the joint, and sequestration.

(4) Fibrous tissue changes, such as extreme proliferation through the joint, bands across the joint, a thickening of the popliteal tissues and a replacement of cartilage and bone marrow with fibrous tissue.

COMMENT

In the bacteriologic study of the successfully sterilized joints, the group in which 0.5 per cent dextrose gentian was used was sterilized the most quickly, the average time being three days. In two of the four joints, the cultures were sterile in twenty-four hours after the injection of the gentian violet. An explanation of this is that the injections of the gentian followed promptly after the infection, and that 4 per cent dextrose as a medium is more efficient than water or olive oil. In the joints in which 0.25 per cent dextrose gentian was used, the average time of sterilization was thirteen days. In these the injection of gentian did not follow the infection as promptly as in the joints in which 0.5 per cent dextrose gentian was used. In the joints treated with 0.25 per cent aqueous gentian, the average time of sterilization was twenty-one days. Again the gentian was not given as promptly after the infection and the medium for the gentian was not felt to be as efficient as 4 per cent dextrose. When 0.5 per cent olive oil gentian was used, the average time of sterilization was twenty-two days. With this group the gentian was injected promptly after the infection, but the varying factor was the medium. The aspirations showed that the olive oil gentian remained in the joints longer than in the other sterile groups,

so that it must be assumed that the amount of gentian necessary to combat the infection quickly was not available.

In the clinical study of the successfully sterilized joints, the group treated with 0.5 per cent dextrose again stands out as the best in the series. The average limitation of extension was 57 degrees and the average amount of swelling a little less than fair. When 0.25 per cent dextrose was used the average limitation of extension was 85 degrees, and the average amount of swelling slightly more than fair. One joint in this group showed only a slight reaction, with 10 degrees' limitation of extension. The 0.25 per cent aqueous method gave an 87 degree limitation of extension with the amount of swelling being fair, while the 0.5 per cent olive oil method gave the same 87 degree limitation of extension with the swelling slightly more than fair. In the gentian controls, there was an average limitation of extension of 7 degrees. In a separate experiment in which guinea-pigs were used, it was shown that there was a definite limitation of motion and proliferation of fibrous tissue after the injection of gentian violet in strengths of 1 to 200 (0.5 per cent), 1 to 100 (1 per cent) and 1 to 50 (2 per cent). In the unsuccessfully sterilized group, there was an average limitation of extension of 127 degrees with an average amount of swelling of slightly more than moderate, while the *Staphylococcus aureus* controls showed an average of 117 degrees' limitation of extension, with a moderate amount of swelling. The difference in motion and swelling in these groups may have been within the limits of variation; however, the greater reaction in the unsuccessfully sterilized joints may have been accounted for by the reaction of the gentian violet on the joint structures, in addition to the reaction of the infection.

The roentgen-ray changes in the joints in which 0.5 per cent dextrose was used were negligible, there being only a slight clouding of the joint. The changes after the 0.25 per cent aqueous treatment and after the 0.25 per cent dextrose treatment were striking, but less marked after the latter. The largest amount of bone destruction was found in the joints in which 0.5 per cent olive oil was used. This group took the longest time for sterilization; hence, there was a greater opportunity for the infection to create the bone changes. The unsuccessfully sterilized joints and the *Staphylococcus aureus* controls showed the same amount of bone destruction as the sterilized joints in which 0.5 per cent olive oil gentian was used. The gentian controls did not show roentgen-ray changes.

The gross pathologic changes corresponded closely to the clinical and roentgen-ray observations. In general, those joints which showed marked bone destruction in the roentgenograms and clinically extreme limitation of motion were found to have acute inflammatory changes, a marked fibrous tissue reaction and both cartilage and bone erosion.

The one joint opened in the group treated with 0.5 per cent dextrose did not show any disease. This, however, was not typical of this group, for a second joint, sectioned but not opened, showed a moderate erosion of cartilage and bone.

The microscopic pathologic changes were markedly less in the successfully sterilized joints than in the unsuccessfully sterilized ones. The joints in which 0.5 per cent olive oil was used showed by far the most changes in the sterile joints, there being erosion of cartilage, sequestration of bone and a large proliferation of fibrous tissue. The fibrous tissue proliferation presented one of the most interesting pictures of the microscopic study. This was found through the joints, diffusely scattered and in bands; it had caused a thickening of the capsule, and, in places, both the cartilage and bone marrow were replaced by fibrous tissue. The formation of abscesses in the epiphyses of the tibia and femur was striking. Some of these abscesses apparently started in the joint and eroded through the cartilage into the bone. These were found more often in the tibia than in the femur.

SUMMARY

It has been shown experimentally that *Staphylococcus aureus* infections of the knee joints of rabbits can be controlled, in 85 per cent of the cases, with injections of gentian violet into the joints. The knees can be sterilized if the gentian violet is injected promptly and adequately after the onset of the infection. The more quickly the infection is controlled, the less extensive the joint changes. The gentian violet itself causes a certain amount of irritation and reaction in the joints. Four per cent dextrose is found to be a more efficient medium for the gentian violet than sterile water or olive oil. It is not believed that injections of gentian violet alone should be resorted to in the treatment of joints infected with *Staphylococcus aureus*, but that this treatment should supplement proper surgical measures for the eradication of the infection.

CONCLUSIONS

1. Gentian violet has a definite effect in allaying infections with *Staphylococcus aureus* in the knee joints of rabbits.

2. Gentian violet, if administered early enough and in sufficient quantities, will sterilize the joints.

PROTOCOL OF RABBIT EXPERIMENTS

RABBIT 1.—Sex, male; weight, 2 pounds, 7 ounces (1.1 Kg.); age, 3 months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec. 21, 1925. Roentgenograms taken of both knees.

Day 1: Right knee was definitely swollen, with increase in local heat, and slight limitation of motion. There was evidence of tenderness with the right leg held up on walking. Rabbit looked toxic.

Day 2: Joint now showed increase in limitation of motion of approximately 70 degrees. Swelling was about the same, with slightly less tenderness and local heat.

Day 3: Joint showed about the same reaction. Culture from joint positive. Aspirated milky turbid fluid. Roentgenogram of right knee showed a slight haziness about the posterior part of the tibia.

Day 5: Right knee showed an increase in the swelling, with the same amount of motion. Swelling had extended down the leg to the midpoint of the ankle. Limp was still marked but not as sensitive to the touch. Culture from joint showed luxuriant growth.

Day 6: Joint showed same motion and swelling.

Day 10: There was a marked increase in the swelling which was nodular in character about the joint, with 105 degrees' limitation of motion. There was evidence of fluid in the joint, with fluctuancy. The rabbit looked quite sick and emaciated. Weight, 2 pounds, 4 ounces (1 Kg.). Culture from joint positive. Roentgenogram showed an irregularity of the tibia and femur with the joint distended and the patella lifted up, showing an irregularity on the inferior surface.

Day 11: The swelling about the knee was much more marked, with only 20 degrees of motion possible, there being a limitation of 120 degrees of extension. The rabbit looked sicker and more emaciated. The left knee now showed a limit of the last 20 degrees of extension. Culture from joint positive.

Day 22: There was now a nodular swelling down the leg to the ankle joint, as well as that about the joint. Motion the same.

Day 37 (autopsy): Culture from right knee positive for *Staphylococcus aurcus*. Roentgenogram of the right knee showed marked destruction of all the joint surfaces with a destruction of the condyles and a few bony projections about these, also new bone formation about the head of the tibia.

The right knee presented a cauliflower-like appearance, with multiple yellowish abscesses beneath the muscular fascia extending from the upper limit of the quadriceps pouches to the lower third of the tibia. The joint could not be extended beyond 135 degrees. There was a string of fibrous tissue running from the abdominal wall to the knee, holding it up in flexion. The joint was not opened.

Microscopic examination could not be performed because the specimens were lost.

RABBIT 2.—Sex, male; weight, 3 pounds (1.4 Kg.); age, 3 months. Injection of the right ear vein with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec. 21, 1925. A small dentist's drill was then used to traumatize the right knee, this being put into the joint and moved around in all directions with the drill revolving. Roentgenograms were taken of both knees; they were negative.

Day 1: The right knee showed a slight limitation to full extension, with a slight amount of swelling. There was no increase in local heat with no limp on walking. The rabbit, however, looked quite toxic.

Day 2: General condition of the rabbit about the same with no change in the knee.

Day 3: The right knee showed a limitation of 10 degrees to full extension. No swelling. The rabbit was more toxic. Roentgenogram of the right knee showed a slight haziness behind the tibia.

Day 5: Right knee showed same amount of motion with slight amount of swelling. The animal looked more toxic and much less lively.

Day 6: Right knee showed slightly more swelling with slightly more limitation to full extension. Otherwise rabbit was the same.

Day 10: Rabbit looked quite emaciated, having lost 15 ounces (0.5 Kg.) in ten days, and seemed toxic. There was now an ankylosis of the right knee in about 75 degrees' flexion, with only a slight amount of swelling. The animal squealed when the left knee was touched, there being a slight amount of swelling and a limitation of the last 20 degrees of extension. Culture from right knee positive. Roentgenogram of the right knee showed a clouding behind the tibia and in the supracondylar region in front.

Day 11: The right knee seemed slightly more swollen and fluctuant, but the general condition of the rabbit was the same.

Day 15 (autopsy): The rabbit died after being much more toxic during the preceding two days. Culture from right knee joint positive for *Staphylococcus aureus.* Culture from heart's blood positive for *Staphylococcus aureus.* Roentgenogram of the right knee showed about the same clouding with small shadows in the anterior joint space.

The rabbit was extremely dehydrated. The right knee was ankylosed at an angle of 75 degrees, with no evident swelling. When the joint was opened, the surfaces were found to be dull and covered with a sticky purulent exudate. The joint was not examined closely. Small abscesses were found in the liver, kidneys, chest wall and leg muscles.

Microscopic examination of a section from the right knee revealed a marked irregularity of the opposing joint surfaces with a destruction in spots of the cartilage. Two abscesses were present in the tibia, one in the epiphyseal line proper and the other in the epiphysis. There was a rather marked leukocytic infiltration with necrotic tissue in the joint and surrounding tissues. An abscess was seen in the opposing surface of the femur. This seemed to open into the joint. The cartilage destruction was certainly more marked over the opposing surfaces of the femur and tibia. There was a rather marked accumulation of pus in the popliteal space with a distention of the capsule in this region. This joined the abscess in the femur.

RABBIT 3.—Sex, female; weight, 2 pounds, 9 ounces (1.1 Kg.); age, 3½ months. Injection of right knee, Dec. 28, 1925, with 0.1 cc. of twenty-four hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a small amount of swelling, with 10 degrees' limitation of extension and definite increase in local heat. The joint was aspirated, and a luxuriant growth was obtained. Injection of 1 cc. of 0.25 per cent aqueous gentian violet into right knee. Roentgenogram showed a slight clouding about the condyles.

Day 2: Right knee showed the same amount of swelling and motion.

Day 3: No change. Aspiration of joint showed a positive culture.

Day 4: The right knee showed a fair amount of swelling, and 30 degrees' limitation of full extension. Injection of 1 cc. of 0.25 per cent aqueous gentian.

Day 10: Right knee showed same amount of swelling and motion. Aspiration showed a positive culture. Injection of 1 cc. 0.25 per cent aqueous gentian. Roentgenogram showed a clouding about all of the joint lines but no destruction of bone.

Day 21: Right knee showed moderate amount of swelling, with 120 degrees' limitation of extension. Aspiration showed a negative culture. Roentgenogram showed a destruction of the opposing joint surfaces of the tibia, femur and patella, with a marked clouding.

Day 23 (autopsy): Culture of right knee was negative. Roentgenogram of right knee showed the same bone destruction as previously reported.

There was about 120 degrees' limitation of full extension, with a moderate amount of swelling. There was an infiltration of gentian beneath the muscle on the outer side of the tibia for almost its whole length. There were many small yellowish areas over the head of the tibia suggesting tiny abscesses in the muscles and fascia. A definite contracture of the hamstrings was found. When the knee joint was opened, a large amount of grumous purplish material was found, with a large amount of fibrous tissue throughout. Some roughening of the bony surface was noted.

Microscopic examination of a section from the right knee revealed remarkably well preserved joint lines, considering the amount of reaction. There was a large amount of fibrous tissue in the joint, with gentian and leukocytes. On the cartilaginous surfaces of the femur and tibia, deposits of leukocytes, fibrin and necrotic tissue were present. The crucial ligaments were preserved and had the same deposits. A rather heavy fibrous band ran through the joint. There was a thinning and destruction of the cartilage in spots. There was one area which suggested a proliferation of cartilage somewhat similar to a chondrosarcoma. A large amount of gentian and necrotic material was found through the muscles. The cartilage was eroded over the popliteal surface of the femur with beginning abscess formation in the femur. There were a few deposits of leukocytes and necrotic material through the adjacent area of the bone marrow.

Rabbit 4.—Sex, female; weight, 2 pounds, 12 ounces (1.2 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec. 28, 1926.

Day 1: Right knee showed a slight limit to full extension, with no swelling or increase in local heat. There was a slight limp.

Day 2: Knee showed the same condition. Injection of 1 cc. 0.25 per cent aqueous gentian. Roentgenogram showed a slight clouding and irregularity behind the condyles of the femur.

Day 3: The joint had a slight limitation to full extension, about 15 degrees, with slight swelling. Culture from joint showed good growth.

Day 4: The joint showed the same limitation of motion and swelling.

Day 5 (autopsy): The rabbit died after a severe, acute diarrhea with prostration. Culture from right knee joint positive. Culture from heart's blood showed *Bacillus hofmani*. Roentgenograms of the right knee showed a clouding about the joint, especially of the lower femur.

On examination, the right knee showed about 15 degrees' limitation to full extension, with a fair amount of swelling. When the knee was opened, a large amount of thick creamy pus was found, which extended up into the quadriceps pouches. The joint surfaces were not carefully examined. There was no evidence of abscess in any other part of the body.

Microscopic examination of a section from the right knee revealed a remarkably small amount of reaction in the joint. A fair amount of pus and fibrin was present but there was no fibrous tissue in the joint. The cartilage of the tibia and femur did not show erosion. The patella and semilunar cartilages were intact. The subpatellar fat pad was well shown and there was no reaction. There was a moderate engorgement of vessels and leukocytic infiltration in the surrounding tissues. The inflammatory process was not far enough advanced in this region to be acute.

RABBIT 5.—Sex, male; weight, 2 pounds, 10 ounces (1.2 Kg.); age, 3½ months. Injection of right knee, Jan. 6, 1926, with 0.2 cc. of twenty-four hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a small amount of swelling, with 10 degrees' limitation of extension and increase in local heat. Joint aspirated but no growth obtained. Injection of 1 cc. of 0.25 per cent aqueous gentian violet.

Day 2: Right knee showed 90 degrees' limitation of extension, with a fair amount of swelling and increase in local heat.

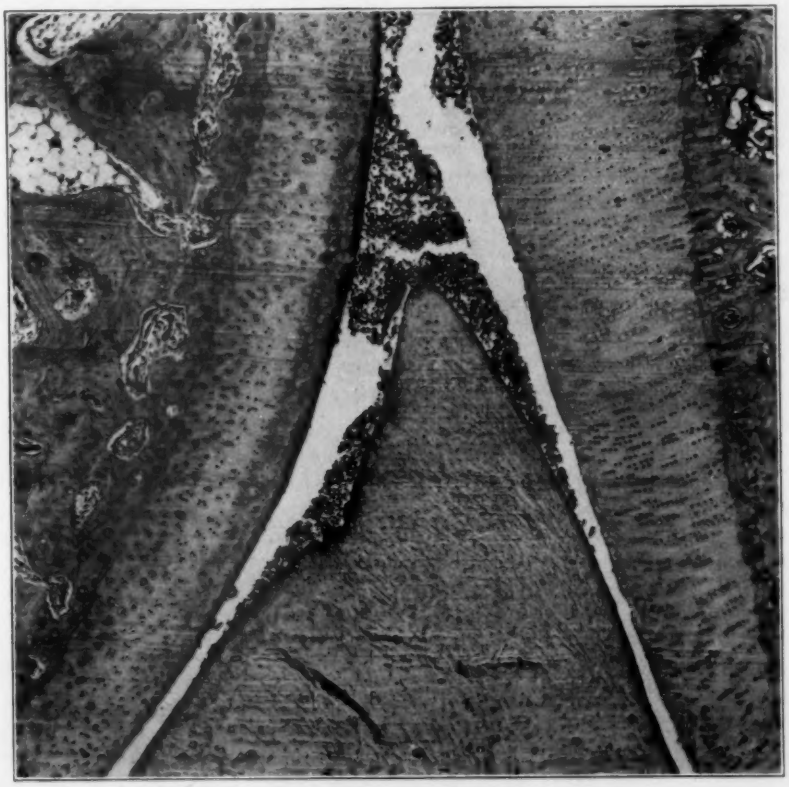

Fig. 6.—Low power photomicrograph of section from rabbit 4. Died on fifth day after infection of acute diarrhea and prostration. Joint culture positive. Joint received one injection of 0.25 per cent aqueous gentian violet on second day after infection. Pus and fibrin in the joint space and a beginning indentation of the cartilage of the tibia (on the right).

Day 4: Right knee showed same amount of motion, with an increase in the amount of swelling.

Day 6: Same as last note.

Day 9: Right knee showed 75 degrees' limitation of extension, with a fair amount of swelling and increase in local heat. Aspiration showed a negative culture. Roentgenogram showed a marked clouding of the joint.

Day 26: Right knee showed 90 degrees' limitation of extension, with a fair amount of swelling. Aspiration showed a negative culture.

Day 51: Right knee showed same amount of motion and swelling. Roentgenogram showed a marked irregularity with a destruction of the joint surfaces and clouding of the joint.

Day 82: Right knee showed the same amount of motion and swelling. Culture from joint negative.

Day 86: Right knee showed 90 degrees' limitation of extension, with a slightly less amount of swelling and no local heat.

Autopsy: Culture from right knee, negative. Roentgenogram of right knee showed a marked destruction of all bony surfaces with a thickening of the head of the tibia and a thinning of the lower end of the femur, with a fusiform shadow along the upper crest of the tibia.

The right knee now showed only 45 degrees of limitation of full extension, with a bony hard swelling along the upper tibia and around the condyles of the femur. On dissection around the joint a small fusiform purplish tinted caseous mass was found along the upper end of the tibia, which gave the roentgen-ray shadow at this point. On section this was found to be a little gritty. When the joint was opened transversely a tremendous amount of fibrous tissue was found in the joint, with a roughening of the upper end of the tibia, and the condyles of the femur. The semilunar cartilages and the crucial ligaments could not be clearly ascertained because of the amount of fibrous tissue.

Microscopic examination of an extremely poor section from the right knee revealed the following: An infiltration of leukocytes could be seen through the joint cavity and muscles, with an engorgement of the vessels. The joint lines could not be determined. No abscesses were seen. The inflammation was apparently slight.

Rabbit 6.—Sex, male; weight, 2 pounds, 12 ounces (1.2 Kg.); age, 3½ months. Injection of right knee, Jan. 6, 1926, with 0.1 cc. of twenty-four hour broth culture of *Staphylococcus aureus*.

Day 1: Right knee showed only a small reaction, with about 10 degrees of limitation of extension and a slight swelling.

Day 4: Same as on first day.

Day 9: The right knee seemed slightly more swollen, with a limitation of the last 20 degrees of extension. Aspiration showed a negative culture. Injection of 1 cc. of 0.25 per cent aqueous gentian violet. Roentgenogram showed a slight clouding about the joint.

Day 24: Right knee a limitation of the last 35 degrees of extension, with a small amount of swelling. Aspiration showed a negative culture.

Day 51: Right knee showed 35 degrees' limitation of extension and same amount of swelling. Roentgenogram showed a slight clouding of the joint with an irregularity of the under surface of the patella.

Day 82: Right knee showed limitation of last 5 degrees of extension, with slight swelling.

Day 86: Right knee showed same amount of motion with a hard swelling around the condyles of the femur.

Autopsy: Roentgenogram showed a slight irregularity of the upper surface of the tibia, lower surface of the femur and under surface of the patella.

There was a slight limitation of full extension of 15 degrees, with no perceptible swelling about the joint. Gentian was not found in the tissues. The joint was not opened.

Microscopic examination of a section from the right knee revealed unusually clear joint lines. There was a slight erosion of cartilage on the opposing surfaces, with a small amount of pus and fibrin in the joint. Gentian was not seen

in the joint or tissues. There was a slight engorgement of the vessels. The patella apparently was normal. A slight amount of fibrous tissue supplanted the bone marrow in the femur. There was a cartillage proliferation from the popliteal side of the tibia. The inflammatory process was like one which has healed.

RABBIT 7.—Sex, male; weight, 2 pounds, 14 ounces (1.3 Kg.); age, 3½ months. Injection of right knee, Jan. 11, 1926, with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed no limitation of motion, with a slight amount of swelling with no increase in local heat.

Day 4: Right knee showed a limitation of 45 degrees of extension, with a fair amount of swelling and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.25 per cent aqueous gentian violet. Roentgenogram showed a slight clouding of the joint.

Day 9: Right knee showed the same amount of motion and swelling. Culture from joint positive.

Day 10: Right knee showed the same. Injection of 1 cc. of 0.25 per cent aqueous gentian.

Day 19: Right knee showed a much more marked reaction, with 110 degrees' limitation of extension and much more swelling, with an increase in local heat. Culture from joint was negative.

Day 38: Right knee showed limitation of extension of 135 degrees, with a moderate amount of swelling. Culture from joint negative.

Day 46: Right knee showed about the same amount of motion and swelling. Roentgenogram showed a marked irregularity of all joint surfaces, with a thinning of the lower end of the femur and a clouding about the joint.

Day 52 (autopsy): Culture from right knee was negative.

The skin over the right knee showed a subcutaneous fibrous reaction. There was a limitation of 90 degrees of full extension. Caseous nodules were present about the upper end of the tibia, in the popliteal space and down the outside of the tibia. This latter was fusiform, and purplish tinted. The popliteal swelling seemed to communicate with the joint proper. When the joint was opened, the most noticeable observation was the amount of fibrous reaction and imperceptibility of the joint structures. There was an erosion of the cartilage and bone in the joint.

Microscopic examination of only a fair section from the right knee revealed the following: There was a marked irregularity of the joint surfaces with erosion of cartilage. Little cartilage remained. A large amount of fibrous tissue was seen through the joint, with pus and fibrin. One large abscess was found in the medullary cavity of the tibia and two small ones in the diaphysis close to the epiphyseal line. Gentian was not seen. One of the abscesses in the tibia apparently connected with the joint. The bone marrow in places had been supplanted by fibrous tissue. The inflammatory process was certainly still in the acute stage.

RABBIT 8.—Sex, female; weight, 2 pounds, 13 ounces (1.3 Kg.); age, 3½ months. Injection of right knee, Jan. 11, 1926, with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed 10 degrees' limitation of full extension, with a slight amount of swelling, and increase in local heat. Injection of 1 cc. 0.25 per cent aqueous gentian violet.

Day 4: Right knee showed 20 degrees' limitation of extension, with a fair amount of swelling and increase in local heat. Culture from joint was positive. Roentgenogram showed a slight clouding of the joint structures.

Day 9: Right knee showed same condition. Injection of 1 cc. of 0.25 per cent aqueous gentian.

Day 11: Right knee showed more marked reaction, with only 90 degrees' extension and slightly more swollen, with swelling in nodules above the patella. Culture from joint positive.

Day 19: Right knee showed limitation of 120 degrees' extension, with about the same swelling and local heat. Culture from joint positive.

Day 21: Knee showed same condition. Injection of 1 cc. 0.25 per cent aqueous gentian.

Day 22: Right knee showed a slight increase in swelling with same motion and increase in local heat. Culture from joint negative.

Day 38: Knee showed same amount of swelling and motion. Culture from joint negative.

Day 46: Knee now showed a limitation of 75 degrees of motion, with same swelling. Roentgenogram showed a marked destruction of the joint surfaces, especially the condyles of the femur and the under surface of the patella, with a few shadows around the joint suggesting gentian infiltration in the tissues.

Day 52 (autopsy): Culture from joint negative.

There was a fibrous reaction in the subcutaneous tissue around the right knee with a slight adherence of the skin. There were many purplish tinged caseous nodules in the fascia, and extending down into the popliteal space. The joint was opened transversely. A large amount of fibrous tissue in the joints bound other elements down tightly. The cartilages were eroded and the bony surfaces were roughened. Gentian was not found in the joint, and there was no evidence of frank pus in the joint. There was a contracture of the hamstrings.

Microscopic examination of a poor section from the right knee disclosed the following: There was a fair amount of fibrous tissue reaction with infiltration of pus about the joint. An infiltration of pus and gentian was observed in the muscles, with an engorgement of vessels.

Rabbit 9.—Sex, female; weight, 3 pounds, 5 ounces (1.5 Kg.); age, 3½ months. Injection of right knee, Jan. 16, 1926, with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a slight amount of swelling, with limitation of 15 degrees' extension and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.25 per cent aqueous gentian violet.

Day 2: Right knee showed slight increase in swelling, with 20 degrees' limitation of extension and increase in local heat. Culture from joint positive. Roentgenogram showed a slight clouding of the joint.

Day 3: Right knee showed 90 degrees' limitation of extension, with slight increase in swelling.

Day 4: Right knee showed same size and amount of motion. Injection of 1 cc. 0.25 per cent aqueous gentian.

Day 6: Right knee showed 100 degrees' limitation of extension, with swelling well up into the suprapatellar pouches Culture from joint positive.

Day 14: Right knee had a limitation of 120 degrees' extension, with swelling more marked, there being nodules to the medial side of the joint. Culture from joint positive.

Day 33: Right knee showed 100 degrees' limitation of extension, with moderate amount of swelling. Reaction was less than last note. Culture from joint showed only one colony of *Staphylococcus aureus.*

Day 41: Right knee showed same swelling and motion. Roentgenogram showed a marked destruction of the joint with a thinning of the condyles of the femur and a thickening of the upper end of the tibia, and a clouding of the whole joint.

Day 53 (autopsy): Culture from right knee negative.

Gentian or pus was not discovered in the surrounding tissues. When the joint was opened the large amount of fibrous reaction in the joint was most marked. All the cartilages were destroyed with a roughening of all bony surfaces. The fibrous tissue had completely filled the joint. Pus or gentian were not found in the joint.

Microscopic examination could not be performed because the specimens were lost.

RABBIT 10.—Sex, male; weight, 3 pounds, 8 ounces (1.6 Kg.); age, 4 months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan. 16, 1926.

Day 1: The right knee showed a slight amount of swelling, with increase in local heat, tenderness and limitation of the last 15 degrees of extension. The rabbit looked toxic.

Day 2: Right knee was more swollen, with more local heat increase and limit to last 30 degrees' extension. Roentgenogram showed a slight clouding about the knee joint. Culture from joint showed moderate growth. Injection of 1 cc. of 0.25 per cent aqueous gentian.

Day 3: Knee joint showed a fair amount of swelling, with limit of 90 degrees' extension and more increase of local heat. Rabbit had lost weight. Weight, 3 pounds, 2 ounces (1.4 Kg.). Culture from joint positive. Aspirated cloudy bloody fluid.

Day 4: Knee was same as on third day. Injection of 1 cc. 0.25 per cent aqueous gentian.

Day 6: The right knee showed more swelling, this being marked in the suprapatellar pouches, with same amount of motion. Culture positive from joint. Aspirated thick purulent material which was slightly purple.

Day 14: Knee was more swollen, with limit of 110 degrees' full extension with fluctuant swelling up into pouches above the knee. Weight, 2 pounds, 14 ounces (1.2 Kg.). Culture from joint showed good growth of organism.

Day 33: There was 120 degrees' limit to motion, with moderate amount of swelling. Culture from joint positive.

Day 41: Right knee showed same swelling and motion with more crepitation about the joint. Roentgenogram showed a marked destruction about the joint with a thinning of the condyles of the femur and thickening of the upper end of the tibia, with evidence of destruction on the under surface of the patella. Some shadows were also seen behind the joint.

Day 72: A moderate amount of swelling was present about the joint, with nodule formation and a limit of 120 degrees of extension. Culture showed a good growth of the organism. Aspiration of thick grumous material.

Day 76: The right knee showed the same nodular swelling, especially on the inner side of the joint, with a thickening of the upper tibia.

Autopsy: Culture from right knee positive.

There was a marked swelling about the right knee in large nodular masses, which contained creamy yellow material, especially on the inner upper aspect of the lower part of the leg. Extension was not possible beyond 120 degrees. When the joint was opened a thinner caseous material was encountered. There was a large amount of fibrous tissue throughout the joint with a lateral disloca-

tion of the patella. There was a marked destruction of all cartilage with a roughening of the bone. A small depression was seen in the intercondylar space. Gentian tinted caseous material was found in the popliteal space extending up toward the joint.

Microscopic examination of a poor section of the right knee disclosed the following: Joint outlines could not be determined. There was an infiltration of pus with an engorgement of the vessels in the muscles. There was one large abscess fairly well encapsulated.

RABBIT 11.—Sex, female; weight, 2 pounds, 10 ounces (1.25 Kg.); age, 4 months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan. 21, 1926.

Day 1: Right knee showed moderate amount of swelling, with increase in local heat and 20 degrees' limit to extension.

Day 6: Joint showed slight tenderness, increase in local heat and 75 degrees' limit to extension, with tenderness. Culture from joint positive.

Day 9: Joint showed a definite increase in the amount of local heat with about same swelling and slightly less motion.

Day 28: Knee showed tumor swelling on outer lower quadrant, with tenderness marked. The rabbit squealed on manipulation of the joint. Motion not beyond 110 degrees' extension. Weight, 2 pounds, 7 ounces (1.1 Kg.). Culture from joint positive.

Day 36: Knee showed marked nodular swelling, especially over the outer lower quadrant, extending down the leg. Motion was limited to 120 degrees. There was an increase in local heat and tenderness. Weight, 2 pounds, 9 ounces (1.2 Kg.). Roentgenogram showed a marked destruction about the joint, with a thinning of the condyles of the femur and thickening of the upper end of the tibia, also roughening of the under surface of the patella with small loose pieces of bone in the popliteal space.

Day 42 (autopsy): Culture from joint positive.

There were small nodular masses on the outer side of the right knee. There was a contracture of the knee to 90 degrees and of the hip to the same, with contraction of both the hamstrings and the quadriceps. The right knee was now opened across the patellar tendon. The cartilage was denuded over all the condyles, with a roughening of the bone. Creamy pus was present in a trabeculated sac in the joint, with much fibrous tissue and new bone formation in the joint.

Microscopic examination of a fair section of the right knee revealed the following: There was a slight amount of fibrin and pus in the joint. The crucial ligament stood out clearly and seemed thickened. There was a slight erosion of the cartilage of the tibia; that of the femur seemed almost normal. The patella was intact. There were several loose pieces of bone in the joint. The joint was marked by the absence of a fibrous reaction. The inflammatory process was in the stage of healing.

RABBIT 12.—Sex, male; weight, 3 pounds (1.4 Kg.); age, 4 months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan. 21, 1926.

Day 1: There was a slight swelling with no tenderness, increase in local heat or limitation of motion in the knee.

Day 6: The right knee showed a slight amount of swelling, with limitation of 45 degrees' extension. Culture showed heavy growth of organism.

Day 9: The right knee was more swollen with increase in local heat and limitation of motion.

Day 28: There was a moderate amount of swelling with 110 degrees' limit to extension, with marked tenderness. The rabbit squealed on manipulation. Culture, no growth.

Day 36: There was now 120 degrees' limit to extension, with swelling about the same. Rabbit walked with the leg drawn up. Weight, 2 pounds, 9 ounces (1.1 Kg.). Roentgenogram showed marked irregularity of joint surfaces, with thinning of the condyles of the femur and thickening of the tibia, roughening on the under surface of the patella and small pieces of bone in the popliteal space.

Day 42 (autopsy): Pus was not visible in the tissues and there were no nodules, as in the other control rabbits. The extension of the hip and knee was limited to 90 degrees. When the joint was opened creamy yellow pus with some gelatinous material was found. The cartilage was pretty much destroyed, with roughening of the condyles of the femur. There was fibrous tissue in the joint.

Microscopic examination of a section of the right knee showed a marked irregularity of all joint lines with a rather generalized destruction of the cartilage. Areas on the tibia and femur showed definite bone involvement and destruction. The joint was filled with pus and fibrin, with a large amount of fibrous tissue all through. Bands of fibrous tissue were seen between the femur and tibia. Islands of cartilage cells were found in the fibrous tissue. Abscesses were not made out in the bone. The patella showed an irregularity of the under surface, with evidence of fibrous tissue. Leukocytic infiltration was present through the surrounding tissues. There was a large amount of pus and fibrous tissue in the popliteal space. The bone marrow in places had been supplanted by fibrous tissue. The inflammatory process was still in a fairly acute stage.

RABBIT 13.—Sex, female; weight, 3 pounds (1.4 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on March 1, 1926.

Day 1: Right knee showed definite increase in local heat, with swelling and 5 degrees' limit to motion. Culture from joint showed good growth. Injection of 1 cc. of 0.25 per cent dextrose gentian heated to 55 C. (131 F.).

Day 4: Right knee showed a large amount of swelling, with increase in local heat and crepitation of the joint. Motion limited to 110 degrees. Culture from joint positive. Aspirated thick purple material. Roentgenogram showed a slight clouding of the joint.

Day 5: Joint showed same amount of swelling, with 120 degrees' limit to full extension. Injection of 1 cc. of 0.25 per cent dextrose gentian.

Day 10: Joint showed same reaction. Weight, 2 pounds, 12 ounces (1.2 Kg.). Culture from joint positive.

Day 28: Joint was moderately swollen, with evidence of fibrous reaction about, and limit of 135 degrees' extension. Culture from joint showed growth.

Day 32: The knee showed the same motion and swelling, with an additional soft fluctuant swelling below the knee.

Autopsy: Culture from right knee positive.

There were many caseous nodules surrounding the right knee with purulent material softer than that in the ones previously reported. There was a marked contraction of the hamstrings preventing extension beyond 135 degrees. Some gentian was found in the caseous material in the popliteal space. The joint was not opened.

Microscopic examination of a section of the right knee showed clearly the destruction and fibrous tissue reaction in the joint. Several large encapsulated abscesses were seen anterior to the head of the tibia. There was a marked erosion of the cartilage along the anterior and posterior parts of the femur and

over the top of the tibia. A great deal of fibrous tissue was observed through the joint, in parts of which were nests of cartilage cells. Fibrous tissue had completely replaced the cartilage along the borders of the femur. A large fibrous band was found across the joint at one side. Pus and fibrin were seen all through the joint. The anterior border of the tibia was eroded by an abscess which had arisen in the soft tissue. The fibrous tissue was supplanting the bone marrow in places. The inflammatory process was one which was subsiding.

RABBIT 14.—Sex, male; weight, 3 pounds, 8 ounces (1.6 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 1, 1926.

Fig. 7.—High power photomicrograph of section from rabbit 13. Autopsy on thirty-second day after infection. Joint culture positive. Joint received two injections of 0.25 per cent dextrose gentian violet. Margin of cartilage erosion with island of cartilage surrounded by fibrous tissue, fibrous tissue proliferation in the joint space and fibrous tissue replacing the cartilage of the bone marrow.

Day 1: Right knee showed a marked increase in local heat, with some swelling and 5 degrees' limit to full extension. Rabbit seemed fairly toxic. Culture showed good growth. Injection of 1 cc. 0.25 per cent dextrose gentian at 55 C. (131 F.).

Day 4: Joint showed moderate amount of swelling, with 100 degrees' limit to extension, with increase in local heat and crepitation. Culture from joint positive. Roentgenogram showed no changes.

Day 5: Joint showed slightly less motion, about 120 degrees' limitation, with same swelling and increase in local heat. Injection of 1 cc. of 0.25 per cent dextrose gentian.

Day 10: Joint showed same changes. Weight 2 pounds, 13 ounces (1.2 Kg.). Culture from joint did not show growth.

Day 28: Right knee showed a surrounding fibrous reaction, with moderate swelling and 135 degrees' limit to motion. Culture from joint positive.

Day 32: Knee showed same swelling and motion. Weight 2 pounds, 10 ounces (1.15 Kg.).

Autopsy: Culture from joint positive.

Several caseous nodules tinted with gentian were found about the joint and in the popliteal space. There was a contraction of the hamstrings. A large amount of bony swelling in the joint could be palpated. The joint was not opened.

Microscopic examination of section of the right knee revealed the following: This was another section which showed well the reaction and destruction of

Fig. 8.—Photomicrograph of section from rabbit 14. Autopsy on thirty-second day after infection. Joint culture positive. Joint received two injections of 0.25 per cent dextrose gentian violet. Four distinct abscesses in epiphysis of femur, an abscess behind the head of the tibia, a necrosis of the posterior portion of the epiphysis of the tibia, pus along the anterior margins of the femur and tibia and pus with necrotic tissue in the joint space. This is the section of roentgenogram *D* in figure 4.

the joint. Abscesses were seen in the popliteal space and in the epiphysis of both the tibia and femur. Those in the femur were linked together and were about four in number. There was a marked fibrous reaction through the joint with pus and fibrin. A layer of pus was seen along the anterior border of both the femur and the tibia. Small islands of cartilage were embedded in the fibrous tissue and pus. There was a destruction of all the cartilaginous surfaces, but it was more marked on the femur. A small sesamoid bone was found in the popliteal space adjacent to an abscess. The bone marrow was supplanted in places by fibrous tissue. The reaction in the joint was that of a fairly acute inflammation.

RABBIT 15.—Sex, male; weight, 2 pounds, 15 ounces (1.4 Kg.); age, 4 months. Injection of the right knee with 1 cc. of 0.25 per cent dextrose gentian violet on March 2, 1926.

Day 1: No reaction could be made out in the knee.

Day 5: There was a slight limitation of extension. No swelling, and no increase in local heat.

Day 32: The right knee showed a slight amount of swelling, with a limitation of the last 10 degrees of extension. Roentgenogram did not show joint changes, but a slight shadow in the popliteal space.

Autopsy: When the skin was removed, the joint had the normal healthy appearance with a gloss to the patellar tendon. When the joint was opened this was essentially normal. There was a slight roughening of the cartilaginous surfaces. All ligaments and other cartilages were normal. A small pocket of gentian was found in the popliteal space. There was about 5 degrees' limitation to extension.

Microscopic examination of the right knee disclosed the following: The cartilage was regular. There was no evidence of any reaction in the joint. A few pus cells and fibrin were present in the joint. The section was only fair.

RABBIT 16.—Sex, female; weight, 3 pounds, 9 ounces (1.6 Kg.); aged, 3½ months. Injection of the right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 5, 1926.

Day 1: Right knee showed a slight amount of swelling, with increase in local heat, and about 5 degrees' limitation to extension. Culture from joint positive. Injection of 1 cc. of 0.25 per cent dextrose gentian.

Day 3 (autopsy): Culture from right knee positive. Roentgenogram of the right knee did not show any changes. The rabbit died without any apparent cause, with no evidence of diarrhea or prostration as seen in rabbit 4.

When the joint was removed there remained only the last 10 degrees of extension, limited, with little swelling. A fair amount of the gentian was found in the muscles of the lower thigh in the popliteal space. When the joint was opened a fair amount of the gentian was present, with an exudate resembling inspissated pus. There was no evidence of fibrous tissue reaction in the joint. Synovial membrane seemed eroded over the condyles of the femur and beneath the patella.

A rather generalized congestion of all organs, the liver, kidneys, heart and lungs was found. A greenish stain was present over the right abdominal wall.

Microscopic examination of a section from the right knee revealed a little reaction in the joint. A small amount of gentian was present and in the surrounding muscles. A few leukocytes were present in the joint and a great many in the muscles. There was a slight irregularity of the cartilage along one border of the femur. Fibrous tissue was not present in the joint.

RABBIT 17.—Sex, male; weight, 3 pounds, 2 ounces (1.45 Kg.); age, 3½ months. Injection of right knee, March 5, 1926, with 0.1 cc. of a 24 hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a slight amount of swelling, with an increase in local heat and 10 degrees' limitation of extension. Culture from joint positive. Injection of 1 cc. of 0.25 dextrose gentian violet.

Day 6: Right knee showed a slight increase in swelling and about the same limitation of motion.

Day 20: There was about 60 degrees' limitation of extension in the knee, with a slight increase in swelling. There was a definite contraction of the hamstring.

Day 24: Right knee showed the same motion and swelling. Culture from joint showed a small growth.

Day 28: There was slight increase in the restriction of motion, with same amount of swelling.

Autopsy: Culture from right knee negative. Roentgenogram of right knee showed a marked irregularity of all joint surfaces with destruction, and a thinning of the condyles of the femur.

A few small nodules of caseous material were seen around the borders of the joint. When the joint was opened a small amount of moderately thick purulent material was found. A beginning destruction of the cartilage was observed on the surfaces of the femur and tibia. The semilunar cartilages and crucial ligaments were clearly demonstrable with little evidence of any change. The extension of the joint was limited 45 degrees. No evidence of gentian was made out in the tissues or the joint.

Microscopic examination of a section of the right knee, showing only the femur and patella, disclosed the following: The cartilage showed a slight irregularity, with a small amount of fibrin adherent. A few leukocytes were seen in the tissues with a small amount of gentian. There was an increase in the amount of fibrous tissue in the popliteal space. The inflammatory process was slight.

Rabbit 18.—Sex, male; weight, 3 pounds, 10 ounces (1.65 Kg.); age, 3½ months. Injection of right knee with 1 cc. of 0.25 per cent dextrose gentian violet on March 6, 1926.

Day 1: There was no swelling or limitation of motion. No increase in local heat.

Day 5: There was limitation of the last 5 degrees' extension. No swelling.

Day 23: Right knee showed limitation of last 5 degrees' extension, with no swelling or increase in local heat.

Day 28: Limitation of motion or swelling could not be made out. Roentgenogram did not show joint changes, but there was a slight shadow in the popliteal space.

Autopsy: The right knee, when the skin was removed, showed a normal glossy appearance. There was about 10 degrees' limit to full extension. All the ligaments and cartilages in the joint were normal. A small pocket of gentian was found in popliteal space.

Microscopic examination of a section of the right knee showed little reaction. There was one break in the cartilage at the lower margin of the femur which was probably an artefact, all of the remaining cartilage being normal. A few leukocytes were found through the muscles. A small amount of fibrin was seen in the joint. Some gentian was observed in the joint and tissues. There was a sesamoid bone in the popliteal space.

Rabbit 19.—Sex, female; weight, 3 pounds, 1 ounce (1.4 Kg.); age, 3½ months. Injection of right knee with 1 cc. of a 0.5 per cent olive oil gentian preparation on March 6, 1926.

Day 1: Swelling, increase in local heat or limitation of motion could not be made out.

Day 5: Joint was essentially unchanged.

Day 23: Knee joint was still the same. Weight, 3 pounds, 7 ounce (1.6 Kg.).

Day 27: Joint still showed no changes. Roentgenogram of the right knee showed no changes.

Autopsy: The right knee had the normal glossy appearance without swelling or external evidence of reaction. There was not any limitation of motion

in the joint. The cartilages and ligaments were normal throughout. Changes could not be made out.

Microscopic examination of a section of the right knee disclosed little reaction. There were a few breaks in the cartilage of the femur and tibia which were probably artefacts. A slight amount of fibrin was found in the joint, and a small amount of gentian. There was a sesamoid bone in the popliteal space.

Rabbit 20.—Sex, male; weight, 3 pounds, 12 ounces (1.7 Kg.); age, 4 months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 11, 1926.

Day 18: Right knee showed a large amount of swelling, with increase in local heat and 100 degrees' limit to full extension. Culture from joint positive.

Day 23: Knee showed large amount of swelling, especially in the outer lower quadrant of the knee, with increase in local heat and fibrous reaction about the joint. Motion limited 110 degrees. Roentgenogram showed a marked irregularity and destruction of the joint surfaces, with clouding of the joint.

Day 88: The right knee showed a more marked nodular formation about the joint, with the same amount of swelling and limitation of motion. Under iodine technic one or two of the nodules were opened and the pus was evacuated.

Day 115: Same method of evacuation of the caseous pus from three more nodules.

Day 128: The right knee showed the same nodular swelling with soft midpoints to the nodules. Motion was not beyond 110 degrees' extension.

Day 216: There was the same nodular swelling, with pus draining from one or two points. Joint was ankylosed at an angle of 120 degrees.

Day 230: The same nodular swelling was seen, with draining sinuses at two points, and a limit of 135 degrees to extension. Swelling extended into the popliteal space.

Autopsy: A large number of caseous nodules with thick purulent material about the joint extended down the lower part of the leg and into the popliteal space. The joint was large and thickened. There was a large amount of fibrous tissue and new bone formation in the joint. All the joint structures were obliterated with a complete destruction of all the cartilage. There was the barest semblance of crucial ligaments. No frank pus was found in the joint. The patella was large, thick and roughened. Some new bone formation was present in the popliteal space. The motion in the joint was from 160 to 135 degrees.

Microscopic examination of a section of the right knee showed a large number of joint changes. There were two abscesses in the head of the tibia about where the epiphyseal line should be seen. A great deal of pus and fibrous tissue was present through the joint. Cartilage was not present on the lower end of the femur or upper end of the tibia. Small fragments of bone were found in the joint. There were a few islands of cartilage separated from, but adjacent to, the tibia. The bone was eroded in spots at the lower end of the femur. Abscesses were seen in the popliteal space. The inflammatory process looked like one which was healing. The bone marrow in places had been supplanted by fibrous tissue.

Rabbit 21.—Sex, female; weight, 4 pounds, 3 ounces (1.9 Kg.); age, 6 months. Injection of right knee, April 9, 1926, with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus*.

Day 1: Right knee showed a definite increase in local heat, with a slight swelling but no limitation of motion. Culture from right knee positive. Injection of 1 cc. of 0.25 per cent dextrose gentian violet.

Day 3: Right knee showed a slight amount of swelling, with 70 degrees' limitation of full extension and marked increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.25 per cent dextrose gentian.

Day 7: Right knee showed a much more marked swelling which had extended down the whole lower part of the leg to the ankle, with 90 degrees' limitation of extension. There was also some limitation of motion in the ankle. Culture from joint negative. Roentgenogram showed a definite clouding of the joint without destruction.

Day 10: Right knee showed a large amount of swelling, with 100 degrees' limitation of extension. There was a nodular swelling on the outer side of the joint. Culture from joint negative.

Day 19: Right knee showed less swelling, with an increase in the motion so that the extension was only limited 60 degrees. Roentgenogram showed a slight clouding and fuzziness of the joint lines.

Day 31: Right knee was almost completely normal, with only small amount of swelling and only a limitation of 10 degrees of full extension. Roentgenogram of right knee was entirely negative.

Day 123: Right knee showed only the slightest limitation of full extension, not over 5 degrees, with absolutely no swelling.

Day 211: The right knee showed normal motion, with no swelling or limit to extension.

Day 225: The right knee showed no swelling, no limit to extension and was, apparently, a perfectly normal joint. Weight, 4 pounds, 9 ounces (2.1 Kg.).

Autopsy: There was a limit of the last 10 degrees of extension, with a slight fibrous reaction around the joint. Swelling, lateral mobility and pus nodules were not present. There was an erosion of the cartilage on the upper portion of the condyles, with island formation of bits of cartilage. The crucials were present and looked normal. The semilunars looked a little thinner than normal. There was a slight erosion of the cartilage around the top of the tibia on the edges.

Microscopic examination of a section from the right knee showed remarkably little reaction in the joint. A small amount of fibrous tissue was found in the joint. No pus in the joint but some in the surrounding tissues. The crucials were present. The cartilage was denuded in spots over both surfaces of femur and tibia. No abscess formation. Large amount of fibrous tissue in popliteal space. The cartilage had proliferated in spots. The bone marrow was supplanted in places with fibrous tissue but this was not marked. The inflammatory process was distinctly one which had healed.

RABBIT 22.—Sex, female; weight, 2 pounds, 10 ounces (1.25 Kg.); age, 3 months. Injection of the right knee, April 16, 1926, with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a slight increase of local heat and swelling, with 10 degrees' limitation of extension. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 3: Right knee showed about 60 degrees' limitation of extension, with slight amount of swelling and local heat increase. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 4: Right knee showed same amount of motion and slightly more swelling. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 6: Right knee showed 80 degrees' limitation of extension, with same amount of swelling and local heat increase. Culture from joint positive.

Day 7: Knee showed 100 degrees' limitation of extension, with same amount of swelling. Roentgenogram showed a slight clouding of the joint.

Day 18: Knee showed 135 degrees' limitation of extension, with large amount of swelling, especially in the upper pouches of the joint. Culture from joint negative.

Day 24: Joint showed marked swelling extending down the lower part of the leg, with nodule formation, and limitation of 120 degrees' extension. Culture showed a small growth. Roentgenogram showed a marked irregularity of the joint line, with destruction of the joint surfaces and a thinning of the lower end of the femur.

Day 31 (autopsy): Culture showed a negative growth. Roentgenogram showed the same joint changes as were seen in the last roentgenogram, with less clouding about the joint.

When the skin was removed there was a limitation of about 120 degrees of full extension, with nodule formation down the inner side of the lower part of the leg. Some gentian was found in the popliteal space. There was a roughening on the under surface of the patella and on the lower surface of the femur. A small amount of pus was present on the joint. The cartilages were pretty well destroyed. All the crucial ligaments were thinned but not destroyed. There was a great deal of fibrous tissue in the posterior portion of the joint which seemed to limit full extension, with a thickening of the capsule.

Microscopic examination of a section from the right knee did not show the tibia clearly, but the changes in the femur were plain. There was an erosion of all the cartilage, with the exception of a few islands. The cartilage had been replaced by fibrous tissue. There was a large abscess containing islands of cartilage which extended through the epiphyseal line of the femur well encapsulated. There was a good deal of fibrous tissue through the joint. Pus was found through the muscles. The inflammatory process looked like one which was becoming progressively more acute. The fibrous tissue in places had supplanted the bone marrow.

Rabbit 23.—Sex, male; weight, 3 pounds (1.4 Kg.); age, 3½ months. Injection of right knee, April 16, 1926, with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus.*

Day 1: Right knee showed a fair amount of swelling, with increase in local heat and limitation of last 15 degrees of extension. Culture from joint negative. Injection of 1 cc. of 0.25 per cent dextrose gentian violet.

Day 3: Right knee showed moderate amount of swelling, with limitation of 75 degrees of extension. Culture from joint positive. Injection of 1 cc. of dextrose gentian violet.

Day 4: Right knee showed more marked swelling, with 110 degree's limitation of extension and increase in local heat. Culture from joint negative. Injection of 1 cc. of 0.25 per cent dextrose gentian.

Day 6: Swelling of right knee was even more marked, with 120 degrees' limitation of motion and increase in local heat. Culture from joint negative.

Day 7: Right knee showed same swelling and motion. Roentgenogram showed a clouding of the joint with a slight fuzziness of the posterior portion of the tibia.

Day 24: Right knee showed 135 degrees' limitation of extension, with a large amount of swelling which was of the nodular type. Roentgenogram showed a marked clouding of the joint with a destruction of the joint lines and a thinning of the lower femur.

Day 31 (autopsy): Culture from right knee negative. Roentgenogram showed same irregularity and destruction, with more thinning of the lower end of the femur.

There were many nodules about the joint with a swelling of the joint. Gentian was found in the foreleg and about the joint. When the joint was opened a large amount of purplish purulent material was found. The crucial ligaments and semilunar cartilages were thinned but not altogether destroyed. There was only a slight roughening of the cartilage on the under surface of the patella and condyles of the femur. The impression was that not as much reaction had occurred in this joint as in some of the others, with the same amount of swelling and limitation of motion.

Microscopic examination of a section from the right knee revealed a marked reaction in the joint. All the joint surfaces were irregular, with an erosion of joint cartilage, only a small amount being left intact in the anterior part of the femur which had fibrous tissue growing into it. A large amount of pus and fibrous tissue was present in the joint. The bone was eroded in spots. There was one place where the bone and cartilage have sequestrated off. A large abscess was seen in the upper diaphysis of the tibia. There were several abscesses in the popliteal space and pus under the periosteum in the anterior part of the femur. The fibrous tissue was supplanting the bone marrow in places. The inflammatory process was subsiding.

RABBIT 24.—Sex, male; weight, 3 pounds, 8 ounces (1.6 Kg.); age, 3½ months. Injection of right knee, April 19, 1926, with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus*.

Day 1: Right knee showed a slight amount of swelling, with limitation of last 15 degrees of extension and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 2: Right knee showed same amount of swelling, with 20 degrees' limitation of extension and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 3: Right knee showed a much more marked reaction, with more swelling extending down lower part of leg into ankle and foot, with much more local heat and a limitation of 90 degrees of full extension. Culture from joint showed a small growth. Injection of 1 cc. of 0.5 per cent gentian in olive oil.

Day 4: Right knee about the same, with perhaps 100 degrees' limitation of motion. Roentgenogram showed a clouding of the joint.

Day 9: Right knee showed less swelling which now extended only to ankle and not into foot, with 90 degrees' limitation of extension. Culture from joint showed small growth.

Day 15: Right knee showed perhaps less swelling down the lower part of the leg, but the same about the knee, with limitation of 75 degrees' extension. Culture from joint did not show growth.

Day 21: Right knee showed the same swelling, with 70 degrees' limitation to extension. Culture showed a small growth after forty-eight hours. Roentgenogram showed a slight haziness about the joint, with some irregularity and thickening of the lower femur.

Day 28 (autopsy): Culture from joint negative. Roentgenogram showed same picture as last described, with slightly less irregularity.

Before the skin was removed there was about 75 degrees' limitation of motion, with some grating and lateral mobility in the joint. Pus was present in gentian tinted nodules down the lower part of the leg. There was thin mucoid pus in the joint, with small bodies suggesting rice bodies. The liga-

ments looked fairly normal with some roughening of the cartilage. The semilunars looked normal. A peculiar bony nodular swelling was observed on the condyles of the femur.

Microscopic examination of a section from the right knee showed a fair amount of reaction. There was an irregularity of the cartilage mainly of the opposing surfaces. A fair amount of fibrous tissue was found in the joint, with pus and fibrin. The largest part of the cartilage was replaced by fibrous tissue. Fragments of bone and cartilage were present in the joint. There was fibrous tissue in the joint attached to cartilage. The anterior part of the femur was well preserved with cartilage. A sesamoid bone was present in the popliteal space. There was no abscess formation. In places the bone marrow had been supplanted by fibrous tissue. The inflammatory process was in the subacute stage.

Rabbit 25.—Sex, male; weight, 3 pounds, 2 ounces (1.45 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on April 19, 1926.

Day 1: There was a slight amount of swelling in the joint, with increase in local heat and restriction of 25 degrees' extension. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 2: Right knee showed the same reaction. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 3: Right knee showed a limitation of 75 degrees' extension, with same amount of swelling and increase in local heat. Gentian recovered in aspiration. Culture from joint showed a small growth. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 4: There was a more marked reaction with 110 degrees' limitation of extension and the same amount of swelling. Roentgenogram showed a clouding of the joint.

Day 9: There was an increase of the motion to 45 degrees' limitation of extension, with probably more marked swelling and less local heat. No gentian now in the aspiration. Culture from joint showed small colonies of the *Staphylococcus aureus.*

Day 15: The same amount of swelling was filling the outer pouches of the knee, and extension was limited 60 degrees. Culture from joint showed few small colonies.

Day 21: There was less swelling with same motion as last noted. Culture showed one small colony in forty-eight hours.

Day 28 (autopsy): Culture from knee negative. Roentgenogram showed a marked haziness about the joint, with an irregularity of the upper tibia and the lower femur.

There was a large amount of purplish tinged pus in the tissues of the lower part of the leg. The joint capsule was distended with a light mucoid material. There was a limitation of the full extension of 60 degrees. There was a definite grating of the patella on the femur. A moderate amount of swelling was present about the joint. The joint was not opened.

Microscopic examination of a section from the right knee disclosed erosion of the cartilage in several places. The cartilage on the tibia had fibrous tissue growing beneath, and in places along the femur cartilage was growing out into the fibrous tissue. A small amount of pus and fibrin was present in the joint, with a fair amount of fibrous tissue. There were thickened synovial tags. The semilunar cartilages were intact. There was a replacing of the bone marrow with fibrous tissue. The inflammatory reaction was still in the acute stage.

RABBIT 26.—Sex, male; weight, 3 pounds, 4 ounces (1.5 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on April 20, 1926.

Day 1: Right knee showed a slight swelling, with limitation of last 10 degrees of motion and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 2: A marked swelling of the knee extended down the ankle to the foot, with a limitation of 90 degrees of full extension, and an increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 3: Knee showed limitation of 110 degrees' full extension with same swelling down leg to ankle and foot. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian. Roentgenogram showed a slight clouding of the joint.

Day 8: There was more marked swelling of the whole knee, lower part of the leg and foot with motion limited 100 degrees. Culture from joint positive.

Day 14: There was a more nodular swelling around the knee which extended down the foreleg to the ankle. At the ankle there was an open draining sinus from which gentian tinted pus could be expressed. A culture from this showed the same organisms. The motion at the knee and ankle was limited 90 degrees. Culture from knee joint showed positive growth.

Day 20: Right knee showed the same nodular swelling, with a limitation of extension of 100 degrees. The swelling down the leg was not as marked. The motion in the ankle was now limited only 30 degrees. There was a scab over the sinus at the ankle. Culture from knee showed one colony after forty-eight hours. Roentgenogram showed a haziness about the joint surface, with an irregularity of the upper tibia and lower femur, with a thickened nodule on the femur.

Day 27 (autopsy): Culture from knee was negative. Roentgenogram showed same condition as on twentieth day.

A rather large nodular swelling was seen about the joint and a distention of the joint capsule proper. A good deal of caseous looking gentian tinted pus was present in the popliteal space and around the joint, also down the lower part of the leg. There was a definite increase in the mobility of the joint with a grating on motion. The joint was not opened.

Microscopic examination of a section from the right knee revealed a large amount of reaction and destruction in the joint. There was a marked irregularity of the joint surfaces. All the cartilage was eroded except that on the anterior surface of the femur. Fissures were present in the cartilage on the tibia. A large amount of fibrous tissue and pus was found in the joint. There were abscesses anterior to the head of the tibia and in the popliteal space. Thickened synovial membrane in the popliteal area. There was a small sesamoid bone anterior to the femur, which might have been the patella but was not altogether typical of this. Thickened crucial ligaments were present. In places, the bone marrow had been supplanted by fibrous tissue. The inflammatory process was fairly acute.

RABBIT 27.—Sex, female; weight, 3 pounds, 8 ounces (1.6 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926.

Day 1: Right knee showed a fair amount of swelling and increase in local heat, with limitation of 10 degrees' extension. There was also a swelling of the glands in the right groin. Culture from joint positive. Injection of 1 cc. of 0.5 per cent dextrose gentian violet.

Day 2: There was more swelling, with an increase in local heat and limitation of last 45 degrees of extension. Gentian was aspirated from the joint. Culture from joint negative. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 3: Joint showed a slight decrease in the swelling and local heat, and 30 degrees' limitation of motion. Crepitation was present in the suprapatellar pouches. Gentian aspirated. Culture from joint negative.

Day 4: Knee showed same amount of swelling, with crepitation and 45 degrees' limit to full motion. Culture from joint negative.

Day 9: Joint showed same amount of swelling, with no increase in local heat and 100 degrees' limitation of full extension. Culture from joint negative. Roentgenogram showed a slight haziness about the joint.

Day 13: Knee showed slightly less swelling and 90 degrees' limitation of extension. Small amount of caseous gentian tinted tissue aspirated. Culture from joint negative.

Day 18: Joint showed a moderate amount of swelling, with an increase in the size of band running from the joint up to the groin. There was 90 degrees' limit to full extension. Gentian aspirated. Culture from joint negative.

Day 68: The knee showed about the same swelling and a limit of extension of 90 degrees. There was some crepitation of the tissues and a nodule in the upper inner pouch about the joint.

Day 156: The right knee could not be extended beyond 90 degrees. There was no swelling. The rabbit looked sick and emaciated. There was an extensive ulceration over the right buttock extending up to the flank.

Day 160: The rabbit died of malnutrition and weakness. Autopsy was not performed.

RABBIT 28.—Sex, male; weight, 3 pounds, 13 ounces (1.7 Kg.); age, 4 months Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926.

Day 1: Right knee showed a slight amount of swelling, with increase in local heat and 5 degrees' limitation of extension. Culture from joint positive. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 2: Right knee showed a marked amount of swelling which had extended down the whole lower part of the leg into the foot, with 75 degrees' limitation of extension. Culture from joint positive. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 3: Joint showed about the same amount of swelling extending down the leg to the foot, with slightly less limitation of extension to 60 degrees and an increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 4: Joint showed the same amount of swelling with 80 degrees' limitation of extension. Gentian aspirated from joint. Culture from joint negative.

Day 9: Joint showed essentially the same swelling with 90 degrees' limit to full extension. Gentian aspirated. Culture from joint negative. Roentgenogram of joint did not show any changes.

Day 13: Knee showed about the same swelling and motion. Thin gentian aspirated. Culture negative.

Day 18: The right knee seemed much improved, with less swelling and 75 degrees' limit to extension. Thin gentian aspirated. Culture from joint negative.

Day 50: The rabbit died of unknown cause. Autopsy was not performed.

RABBIT 29.—Sex, male; weight, 3 pounds, 5 ounces (1.55 Kg.); age 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926.

Day 1: Right knee showed a slight amount of swelling, with increase in local heat, and about 5 degrees' limitation of full extension. Culture from joint positive. Injection of 1 cc. of a 0.5 per cent dextrose gentian preparation. An extravasation of this took place into the tissues on the inner side of the knee.

Day 2: Knee showed a moderate amount of swelling, with 60 degrees' limitation of extension and marked increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 3: Right knee showed an increase of the same swelling up into the groin with marked crepitation of the tissues and 75 degrees' limitation of full extension. Culture from joint showed a small growth. Gentian aspirated. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 4: Right knee showed the same amount of swelling, which had now extended down into the lower part of the leg, with 90 degrees' limit to full extension. Culture from joint negative. Gentian aspirated.

Day 9: Right knee showed slightly less swelling, with crepitation up into the thigh and 100 degrees' limit to full extension. Cultures from joint negative. Gentian aspirated. Roentgenogram of the right knee did not show any changes in the joint. This picture showed the same appearance of the joint as that taken before infection.

Day 13: Right knee showed fair amount of swelling, with 110 degrees' limit to full extension, crepitus in the joint and a small ulceration below the knee. Weight, 3 pounds, 7 ounces (1.6 Kg.). Culture from joint negative. Gentian aspirated.

Day 18: The right knee showed a marked improvement, with only a small amount of swelling and 60 degrees' limit to full extension. Culture negative. Gentian aspirated.

Day 21 (autopsy): Culture from right knee negative.

There was more than 45 degrees' limit to full extension, with a fair amount of swelling. A purple tinge was present all about the joint when it was opened. An air space was found up in the groin. The gentian was found down the outer side of the lower part of the leg, almost to the ankle. When the joint was opened transversely, it was found to be filled with gentian. Pus was not present in the joint. Close examination of the ligaments and cartilage in the joint revealed no change. The gentian was also in the popliteal tissues. Limitation of motion could not be demonstrated after the joint was opened.

Microscopic examination could not be performed because the specimens were lost.

Rabbit 30.—Sex, female; weight, 3 pounds, 4 ounces (1.5 Kg.); age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926.

Day 1: Right knee showed a slight amount of swelling, with increase in local heat and 5 degrees of limitation of extension. Culture from joint showed good growth. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 2: Knee showed increase in swelling, with increase in amount of local heat and 20 degrees' limit to extension. Culture from joint negative. Aspiration showed gentian. Injection of 1 cc. of 0.5 per cent dextrose gentian.

Day 3: Joint showed slight increase in local heat, with less swelling and 30 degrees' limit to extension. Culture from joint negative. Gentian aspirated.

Day 4: Joint showed 45 degrees' limit to extension and same amount of swelling, with crepitation up into the groin. Culture did not show growth. Gentian aspirated.

Day 9: Right knee showed same swelling, with 75 degrees' limit to extension and little crepitus. Culture from joint was negative; gentian aspirated. Roentgenogram did not show changes.

Day 13: Joint showed same swelling, with less limitation of extension, this being now 40 degrees. The rabbit showed a marked loss of weight. Weight, 2 pounds, 11 ounces (1.2 Kg.). Culture from joint negative. Gentian aspirated.

Day 18: Right knee was almost normal, with just a little limitation of extension, about 5 degrees, and the slightest amount of swelling. Culture negative. Gentian aspirated.

Day 55: There was no limitation of motion, with no swelling. A small scab was seen on front surface of knee beneath which a little pus was found.

Day 68: Knee joint showed a small amount of swelling with about 10 degrees' limitation to full extension.

Day 156: The right knee showed a distinct lateral dislocation with apparent evidence of the crucial ligaments being relaxed. There was about 70 degrees' external rotation with 30 degrees of abduction and 45 degrees' limitation to full extension. Swelling was not present.

Day 170: The knee showed a limit of 90 degrees to full extension, with the same lateral displacement. Weight, 4 pounds, 8 ounces (2 Kg.).

Autopsy: The joint was opened transversely across the patellar tendon. Pus and gentian were not found in the joint. There was a marked erosion of all the cartilage over the condyles of the femur, with small islands of cartilage remaining. Small bits of cartilage were free in the joint. There was also a distinct roughening of the bone. The crucial ligaments were thin and extremely relaxed, and allowed the lateral mobility of the joint. The semilunar cartilages were thin and irregular in contour. There was a slight fibrous reaction on the sides of the joint.

Microscopic examination of a section from the right knee revealed a marked thinning of the femur and thickening of the head of the tibia. There was an irregularity of the cartilage which was destroyed in spots along the joint surfaces. A marked fibrous tissue reaction was seen in the joint, in which there were clumps of cartilage cells. In spots the bone was eroded. The semilunar cartilages were present and intact. The crucial ligaments were much thinner than normal. A sesamoid bone was present in the popliteal space. There was a thickening of synovial membrane. Pus was not present. Slight leukocytic infiltration of the muscle had occurred. The surface of the bone gave the impression of one which has healed. Small villous processes were present in the joint, which had proliferated from the synovial membrane. There was a proliferation of cartilage. Little acute inflammation was seen in this joint.

EXTRAPLEURAL THORACOPLASTY: A MUSCLE SPLITTING OPERATION *

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The Wilms-Sauerbruch operation of extrapleural thoracoplasty is performed as a routine through a single paravertebral incision. The incision extends from the upper border of the trapezius muscle to a point over the eleventh rib, and is carried down through the layers of muscle to the level of the ribs at the outer border of the erector spinae group.

This incision necessitates transverse section of the trapezius, rhomboids and latissimus dorsi, and is consequently bloody and traumatizing. It is certain that it favors postoperative shock and infection of the wound, complications which, as Archibald has recently brought out, account for most of the direct operative mortality.

Furthermore, when the operation is performed in stages, if even a slight infection occurs after the first or second stage, it is necessary to prolong the interval between operations, frequently to such an extent that the resected ribs regenerate and the final collapse is compromised.

It seemed to me that these drawbacks could be obviated and the function of the arm and shoulder better preserved if the operation were performed through separate incisions and the ribs approached by splitting rather than by transecting the broad muscles of the shoulder girdle.

To meet these requirements, the following muscle splitting operation in three stages has been devised:

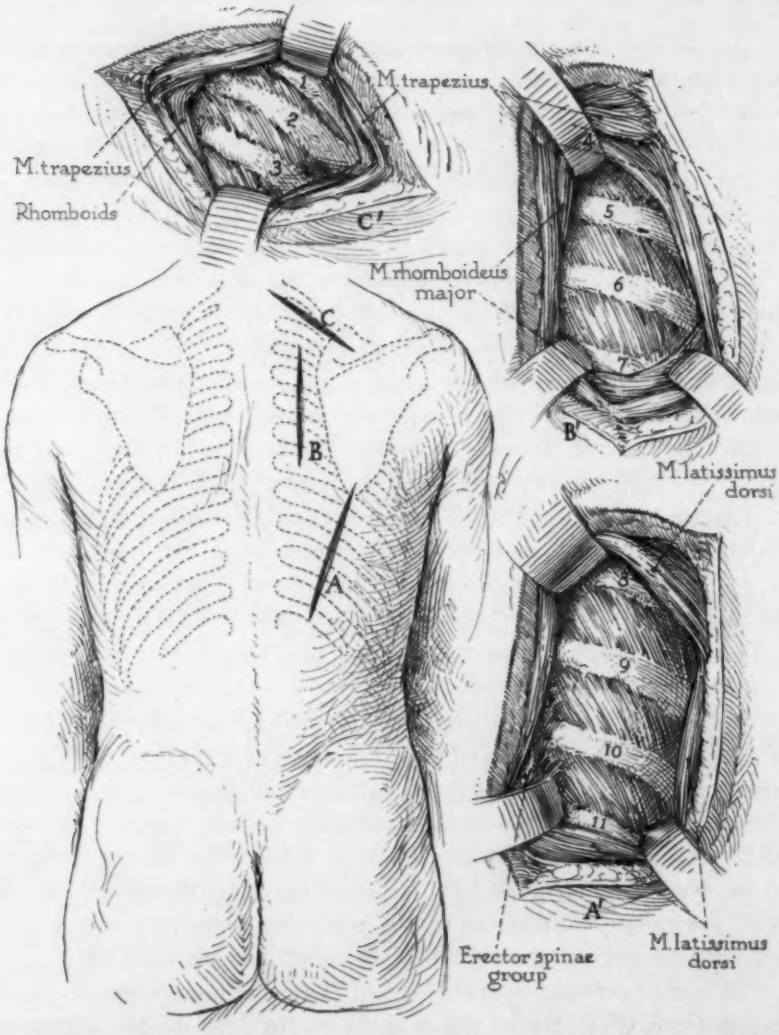
The first incision begins over the eleventh rib just lateral to the spine and runs upward and outward over the angle of the scapula. The skin and subcutaneous tissues are freed from the latissimus dorsi for a short distance on each side of the incision, and this muscle is split in the direction of its fibers. The loose areolar tissue binding the muscle to the ribs and the intercostal structures can be freed easily by the finger, and, this having been done, adjustment of the retraction gives easy access to the posterior segments of the eighth, ninth, tenth and eleventh ribs.

The second incision is in the line of the usual paravertebral one and extends from the spine of the scapula to the level of the eighth rib. Small flaps of skin and subcutaneous tissues are dissected up from the trapezius, and the muscle is split in the line of its fibers. The trapezius is freed on its under surface, and the rhomboid is thus brought into view. This muscle is similarly split and freed from the ribs and under-

* From the Surgical Service of the Research and Educational Hospitals of the Medical School of the University of Illinois.

lying tissues. Adjustment of the retraction gives easy access to the desired segments of the fourth, fifth, sixth and seventh ribs.

The third incision is made in the line of the fibers of the trapezius and extends from the second dorsal spine to the middle of the spine of the scapula; or, in case there has not been infection in the second



A muscle splitting operation in three stages for extrapleural thoracoplasty.

incision, it may be merely extended upward as has heretofore been the practice. Flaps having been raised, the trapezius and rhomboid muscles are split and freed on their under surfaces. Then proper adjustment of the retraction affords access to the posterior segments of the first, second and third ribs.

The two patients on whom this operation has been performed were able to be out of bed the third day after the final stage, and could move the arm and shoulder on the affected side freely in all directions without pain.

SUMMARY

1. The usual paravertebral incision for the operation of extrapleural thoracoplasty has two serious drawbacks:

(*a*) The transverse section of the broad muscles of the back adds to the hemorrhage and trauma and is a factor in postoperative shock, infection and deformity.

(*b*) When the operation is performed in stages, as is usual, infection in one incision necessitates increasing the interval between operations, frequently to such an extent that the resected ribs regenerate and the final collapse is compromised.

2. These drawbacks can be obviated by performing the operation in three stages through separate incisions, and by splitting rather than transecting the broad muscles of the shoulder girdle.

AN EXPERIMENT WITH BROTH CULTURES OF STAPHYLOCOCCUS AUREUS AND GENTIAN VIOLET *

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Following the lines of experimentation of Churchman [1] in 1922, when he showed that a slight increase in temperature had a definite effect on the bacteriostatic power of gentian violet, and of Gatch, Trusler, and Owen [2] in 1925, when they showed that gentian violet in 4 per cent dextrose was less toxic for rabbits than aqueous gentian violet, experiments were performed in test tubes and on agar plates to correlate these facts.

Twenty-four hour broth cultures of *Staphylococcus aureus* containing about 9 cc. of fluid were used. Gentian violet was prepared first

*Reaction of Staphylococcus aureus Broth Culture to Aqueous and 0.25 Per Cent Dextrose Gentian Violet in the Incubator at 37.5 C. and in the Water Bath at 50 C.**

	0 Min.	2 Min.	4 Min.	6 Min.	8 Min.	10 Min.	15 Min.	20 Min.	30 Min.	40 Min.	60 Min.	120 Min.
I. Incubator 37.5 C.												
1. Control	+	+	+	+	+	+	+	+	+	+	+	+
2. Aqueous gentian	+	+	+	+	+	+	+	+	+	+	+	—
3. Dextrose gentian	+	+	+	+	—	—	—	—	—	—	—	—
II. Water bath 50 C.												
1. Control	+	+	+	+	+	+	+	+	+	+	+	—
2. Aqueous gentian	+	+	+	+	—	—	—	—	—	—	—	—
3. Dextrose gentian	+	+	—	—	—	—	—	—	—	—	—	—

* Dilution of gentian violet, 1 to 10,000.

with distilled water as a medium and then with 4 per cent dextrose as a medium. Sufficient amounts of the gentian violet preparations were added to the broth cultures to make a 1:10,000 dilution of the dye. A bath at 50 C. was used to give the increase in temperature. A series of six broth cultures was used, divided as follows: two contained aqueous gentian violet; two 4 per cent dextrose gentian violet, and two controls. One set of three cultures was placed in the incubator at 37.5 C. and one set in the water bath at 30 C. Subcultures were taken immediately before adding the gentian violet, and at periods thereafter of five, ten, fifteen, twenty, thirty, forty, sixty minutes, and two hours.

* From the Louis Bowles Foundation of the Children's Hospital School, Baltimore.

1. Churchman, J. W.: Bull. Johns Hopkins Hosp. **33**:277 (June) 1922.

2. Gatch, W. D.; Trusler, H. M., and Owen, J. E.: Treatment of General Septicemia by Gentian Violet and Mercurochrome-220 Soluble, J. A. M. A. **85**: 894 (Sept. 19) 1925.

Plain agar plates were used for the subcultures. The cultures were noted in twenty-four and forty-eight hours. In the incubator the cultures did not show any growth in the aqueous gentian violet after sixty minutes, nor any growth in the 4 per cent dextrose gentian violet after five minutes. In the water bath there was no growth at any period in either the aqueous or 4 per cent dextrose gentian violet cultures, nor was there a growth in the control culture after sixty minutes. The experiment was now checked and the results obtained, except that in the water bath the aqueous gentian violet showed a growth at five minutes. An attempt was made to determine more nearly the time the cultures became sterile. The same experiment was repeated with subcultures made at two, four, six, eight, ten, fifteen and twenty minute intervals after the addition of the gentian violet. In the incubator there was no growth after six minutes in the 4 per cent dextrose gentian violet, while the aqueous gentian violet showed a growth in all cultures. In the water bath there was no growth after six minutes in the aqueous gentian violet, and no growth after two minutes in the 4 per cent dextrose gentian violet.

From this experiment it is concluded that dextrose gentian violet is more toxic for *Staphylococcus aureus* than aqueous gentian violet, and that heat has a definite effect on the bactericidal power of the gentian violet. *Staphylococcus aureus* is therefore destroyed quicker by gentian violet in 4 per cent dextroses than in sterile water, and in the presence of an increase in the surrounding temperature.

THE TRANSFUSING OF UNMODIFIED BLOOD

IV. EXPERIENCE IN NEARLY TWO THOUSAND, FIVE HUNDRED CASES: CHANGES IN APPARATUS *

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DETROIT

The progress and results of blood transfusion at this clinic, first with the Unger [1] apparatus and then with my modification [2] of the Unger apparatus, have previously been discussed in part by Dr. Blain and me.[3] With these two types of apparatus, which were somewhat similar, nearly 2,500 transfusions of unmodified blood have been performed. The method has proved satisfactory and leaves little to be desired. The method provides for a continuous flow of blood from the donor to the recipient with scarcely any clotting, because stagnation is eliminated. The maximum of speed is acquired, the time necessary for the actual transfusion of 500 cc. being about five minutes. Many of the transfusions have required even less time, and it has never been observed that the blood was given too rapidly. Foreign material is not introduced during the transfusion, with the exception of 3 or 4 cc. of saline before any blood passes through the apparatus, and this is for the purpose of demonstrating the correct position of the needle in the recipient's vein.

There have not been any deaths directly attributable to transfusion in the series. Transfusion may have been a contributing factor in the cause of death in three cases of nephritis. My experience, naturally, added to the observations of others, leads me to suspect that nephritis might constitute a contraindication to transfusion. The only other contraindications are pulmonary edema and a damaged myocardium. Although I have never observed unfavorable consequences following transfusion in cases of heart lesions, I would advise caution.

The criteria of a post-transfusion reaction should include, in addition to a mere elevation of temperature, some definite subjective or objective symptoms, such as a chill, pain, dyspnea, urticaria, hemoglobinuria and jaundice.

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* From the Jefferson Clinic and Diagnostic Hospital.

1. Brines, Osborne A.: The Transfusing of Unmodified Blood. Arch. Surg. **7**:306 (Sept.) 1923.

2. Brines, Osborne A.: The Transfusing of Unmodified Blood: II. The Technique in 1000 Cases, Arch. Surg. **12**:124 (Jan.) 1926.

3. Blain, Alexander W., and Brines, Osborne A.: The Transfusing of Unmodified Blood: III. The Clinical Aspect of 1000 Cases, Arch. Surg. **12**:140 (Jan.) 1926.

In nearly 2,500 cases in which transfusion was used, only three patients had severe post-transfusion reactions. All were purely anaphylactic in type and occurred with sudden onset immediately following the transfusion. One reaction was extremely severe and the other two moderately severe.

One of the less severe reactions consisted of a convulsion followed by coma and accompanied by an increase in pulse rate and a decrease in the volume of the radial pulse, shallow and slowed respirations and cyanosis, all of which lasted about thirty minutes and were immediately followed by complete recovery.

The most severe reaction consisted of a convulsion and then coma, cyanosis and shallow respiration, the respiratory rate dropping to 2 or 3 a minute, and complete disappearance of the radial pulse and inaudible heart sounds. This state lasted about half an hour, after which the pulse and respiration became satisfactory; the patient reacted to his surroundings at the end of an hour, but remained more or less delirious for several hours.

The third reaction occurred in one of the cases of nephritis mentioned, and the initial symptom was a sudden onset of severe generalized abdominal pain which, after about ten minutes, shifted to the lumbar region. The pain was relieved by the administration of morphine sulphate, ½ grain (0.03 Gm.); but a severe chill accompanied by an elevation in temperature of 4 F. followed. The reaction in this form was intermittent and lasted with diminishing severity for about thirty-six hours. Uremic symptoms became conspicuous and death occurred in five days. A careful recheck of grouping and crossagglutination failed to reveal the slightest incompatibility in any of these three cases.

Crossagglutination as a routine procedure was abandoned as unnecessary and superfluous in the laboratory of the Jefferson Clinic four years ago, when we began to use group IV (Moss) agglutinating serum in addition to the usual group II and group III serums. By this means, we are able to detect deterioration of either group II or group III serum. Errors in blood grouping are usually not due to poor laboratory technic but to a sudden reduction in titer of the known serums. It is a well known fact that agglutinating serum may possess sufficient titer today but tomorrow may be absolutely useless. In some laboratories where several days and even weeks may elapse between requests for blood grouping, the serums employed are not reliable without this additional safeguard, which depends on the fact that if there is agglutination with group IV serum, there must be agglutination with either group II or group III serum or both. When agglutination is produced with group IV serum alone, one of the other serums must be impotent, and an investigation can be made. The most common error in grouping, and the only one that I have personally witnessed, is placing a group II

(Moss) individual in group IV, and probably the most important reason for this error is the use of old group III serum due to the difficulty or inconvenience experienced in securing group III serum because of the small number of group III individuals. The use of group IV serum is not an infallible check, but will practically eliminate all error, because it is unlikely that two of the agglutinating serums will deteriorate at the same time; besides, on account of the prevalence of group IV individuals, fresh group IV serum can be obtained frequently—every two or three days—and therefore can be regarded with the greatest confidence.

The only error that cannot be guarded against by the use of group IV serum is that of mistaking a group I for a group II or a group III individual; the reason for this is that the cells of a group I individual are agglutinated by both groups II and III serum, and impotence of one or the other would not be detected by this method. The small number of group I individuals minimizes the importance of this danger, and the possibility of such a mistake argues for the more extensive use of universal donors. Since the introduction of group IV serum in the laboratory as a check on the potency of group II and group III serums, errors in grouping have not been made.

In my experience, incompatible blood was used in six transfusions. Four of these errors in grouping occurred in laboratories other than this one, and two occurred in the laboratory before I began to use group IV serum. No casualties resulted in four cases. In one of the other two, death was inevitable and was perhaps hastened by the transfusion. Suspicion regarding compatibility was aroused by the sudden cyanosis of the patient when about 200 cc. of blood had been introduced. The other case was one of the three cases of nephritis mentioned before. The patient was moribund, and when about 100 cc. of blood had been introduced, dyspnea was suddenly observed. The transfusion was stopped because of the belief that incompatible blood was being used. A severe reaction consisting of a chill and dyspnea occurred, and death followed in three days. In all six cases, group II blood was given to group IV patients. In one case, the error was a clerical one in reporting.

In these two cases just described, one patient was comatose and the other was semiconscious; if the operator is reasonably careful and alert, it is only in this type of case that a fatality may follow the use of incompatible blood. The nervous reaction of these patients is too sluggish to detect or to betray the aura of a transfusion reaction, and before it becomes evident that the patient is not behaving normally, a sufficiently large quantity of blood to produce serious consequences has been given. It is likely that a patient who is fully conscious will inform the operator, who should always have in mind the possibility of using incompatible blood, of the first unusual or uncomfortable sensation, which is commonly lumbar or mediastinal pain or respiratory difficulty. Such warning

symptoms will usually occur before 40 cc. of blood has been given, and if the transfusion is discontinued promptly, nothing more serious than a mild or moderately severe reaction will result.

There is one type of post-transfusion reaction which is seldom mentioned and has received little attention, but which occurs with mild symptoms in a small percentage of cases; that is the delayed reaction. I was slow in appreciating the existence of such a type of reaction, because as a rule I did not observe the occurrence myself, and when I was occasionally told that a patient who had received a transfusion in the morning had a mild or moderately severe chill that night or the next day, lasting sometimes for an hour or more, I was inclined to consider this a mysterious affair unrelated to the transfusion, because I was sure that if a reaction did not occur within two hours, none would occur. The delayed reaction is now recognized but a possible explanation for such a phenomenon cannot be suggested.

As far as I know, embolism has never been produced during a transfusion given by my associates or me. I have never seen a case of air embolism, but I recognize that there is danger of such an occurrence, and I never inject more than a few very small bubbles of air.

In only two cases in this series did the attempt to perform a transfusion fail because of inability to introduce the needle into the patient's vein. The first case was that of an infant, and this incident has been described in a previous article.[2] The second unsuccessful attempt was made in the case of an obese woman who had received two transfusions within the preceding two or three weeks. Both arms had been used, and on each side an incision had been made and the vein exposed but not transected or ligated. The third transfusion for this patient, who was a poor surgical risk, was attempted in the operating room at the end of an abdominal operation. Incisions in the arms were necessary, but a mistake was made in that the new incisions were parallel to the old ones, instead of being started where the previous ones ended. The veins which had been entered before were tried this time, and in each arm the vein parted at the old site of venous puncture when the pressure of the needle was exerted, and the proximal end of the vein could not be picked up and no other veins could be readily found. Before another location could be selected, the patient died. The technic was admittedly faulty, and a different line of attack would be employed in a similar case in the future.

The use of universal donors is becoming more popular continually. One feels safer and less apprehensive of undesirable sequelae when the donor is in group IV. The records show that the smallest percentage of post-transfusion reactions has occurred when the donor has been in group IV, regardless of whether the recipient is in group I, II, III or IV, and the largest percentage of reactions has occurred when both donor

and recipient have been in group II. The work of Guthrie and Huck [4] has shown the possibility of a number of groups in addition to the four which are usually considered, but it is doubtful whether it will ever be necessary to give all of these groups practical consideration. However, in the work in our laboratory, we have long recognized two subdivisions of group II, and I believe that they are of practical importance. My attention was first directed to a difference in the behavior of erythrocytes of different group II individuals when it was observed that in some cases agglutination by group III and group IV serum occurred completely and quickly while in other cases agglutination occurred slowly and incompletely. For lack of a better classification, we began to use the terms "slow twos" and "fast twos." The discovery that the percentage of post-transfusion reactions was nearly twice as great when the donor and recipient were in group II as when any other combination was used leads me to believe that the recognition of "strong and weak twos" were of practical importance. At the present time, we are collecting data on the comparative results produced in the form of post-transfusion reactions when both donor and recipient belong to the same subdivision of group II and when the subgroups are mixed. We advocate the preference of group IV or universal donors in all transfusions when no more than 750 cc. of blood is to be transfused, especially in selecting professional and semiprofessional donors for group II recipients, because of the existence of subdivisions of group II, which are of practical importance and which increase the incidence of reactions. Besides, as I have pointed out, the only real practical error which might occur in blood grouping by the method employed in our laboratory is when one is dealing with group I individuals and the least possibility of error when one is dealing with group IV individuals. This would argue well for the use of group IV donors with patients of groups I and II at least; group III is such a small group that a group III donor is seldom needed, and when needed is seldom found. I therefore feel justified in recommending the preference for group IV donors in all transfusions when practical.

Two questions frequently asked are whether donating blood is harmful to the donor and whether the group of an individual ever changes. I cannot state positively that the repeated withdrawing of blood in 500 cc. quantities is harmful. I have not observed any ill effects. Three of our donors have served between eighty and 150 times over a period of five years, and they are all in excellent health and, as far as I know, specimens of fine physique. Some donors cannot

4. Guthrie, C. G., and Huck, J. G.: Existence of More than Four Isoagglutinin Groups in Human Blood, Bull. Johns Hopkins Hosp. **32**:37 (Feb.) 1923; **34**:80 (March) 1923; **34**: 128 (April) 1923.

give blood as frequently as others without becoming anemic, but the transfusions apparently do not have any permanent ill effects. In our experience or under our observation the group of an individual has never changed. All apparent instances were found on investigation to have been due to an error in grouping.

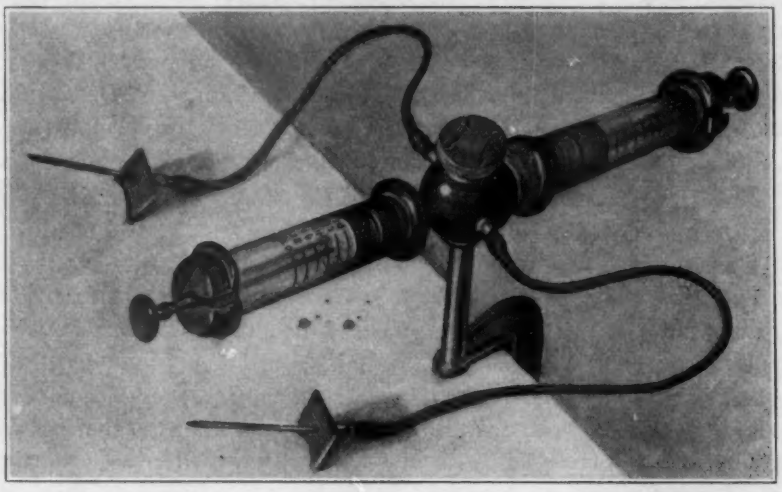

Fig. 1.—The apparatus used in blood transfusions. The arrows indicate the connections with the circulations of the donor and the recipient.

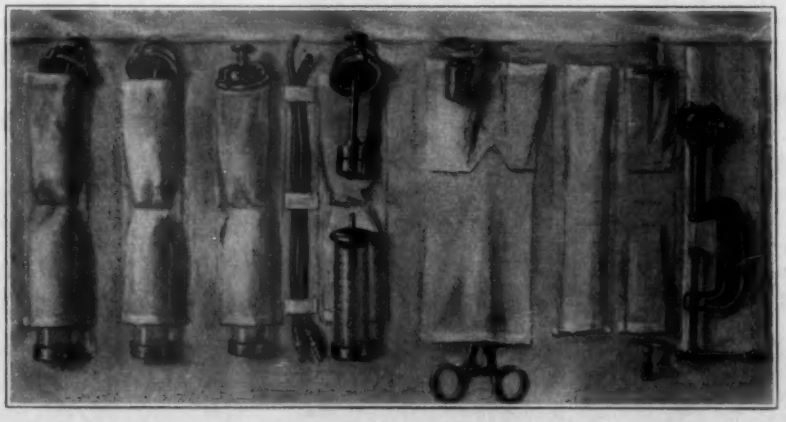

Fig. 2.—Sections of the apparatus in place in their respective compartments in the canvas roll designed for that purpose.

The apparatus which has been used at the Jefferson Clinic and Diagnostic Hospital for the last three years up to a short time ago was a modification described in 1926.[2] This apparatus possessed several minor disadvantages, and we have looked over carefully

the several apparatus placed on the market in the last two years hoping to find one more suitable. All were rejected, however, because of the principle involved or because we believed that our apparatus was more simple, more fool-proof and more accurate. We were not satisfied with any apparatus presented. With these imperfections and undesirable features of the equipment in mind, yet not wishing to make any radical changes or to deviate from the principle involved in the apparatus with which we had performed over 2,000 transfusions, our present apparatus was designed (manufactured by the J. F. Hartz Company, Detroit), the accompanying illustrations of which, I believe, are self-explanatory.

This apparatus possesses the following advantages:

Foreign substance is not mixed with the blood, and the blood is not modified in any way.

The amount of blood can be accurately measured.

The apparatus is small and light and consists of only two parts.

Lubrication of moving parts or paraffin coating is unnecessary.

Veins are entered by needles.

A canvas roll with a separate compartment for every piece of the equipment in which the apparatus can be wrapped immediately after cleaning and autoclaved and in which everything will remain sterile is part of the equipment.

By means of arrows, only a glance is necessary to determine whether the operator's syringe communicates with the circulation of the donor or recipient, and thereby is eliminated the possibility of taking blood from or injecting it into the wrong person.

By means of two syringes working opposite each other and always connected with the opposite side arm of the apparatus, it is possible to provide a continuous stream of blood from the donor to the recipient and thereby to reduce the possibility of clotting to a minimum, because stagnation will not occur in the apparatus.

The donor, or recipient, may be placed on either side of the apparatus.

The actual transfusion can be performed in less than five minutes.

The blood is not unduly agitated, cooled or exposed to the air.

METHOD

The donor and recipient are placed in the supine position about 18 inches apart, with their heads in the same direction, their shoulders opposite each other and with a table or board between them in such a position that the elbows of both the donor and the recipient lie over the board at the edge nearest the foot of the table. The donor is placed on the operating table in the operating room, and the recipient is allowed to remain on the stretcher car. An arm board about 12 inches wide is then placed under the pad on the table and allowed to project 18 inches. The car is then brought up to touch the end of the board. In the patient's home, conditions of the operating room must be simulated by various makeshifts.

The arms are bared to the shoulders, and the skin is cleansed with soap and the usual skin antiseptics. Ordinary sterile precautions are observed. Half inch pure gum rubber tourniquets are used, and the pressure of the donor's tourniquet frequently must be varied during the transfusion to obtain the best flow. The patient's tourniquet is removed as soon as the needle is introduced into the vein

The operator stands between the donor and the recipient facing the head of the operating table, and his assistant stands across the board facing him. The operator clamps the apparatus to the side of the board nearest him.

All syringes, which are 20 cc. Records, are rinsed with saline. One syringe is filled with saline, and the tip is inserted into the opening on the side nearest the assistant. The apparatus is tested with this saline to eliminate obstruction and to demonstrate to the satisfaction of the operator that the needle is properly placed well within the lumen of the recipient's vein. A small amount of saline is allowed to flow slowly into the recipient's circulation while the needle is being introduced into the donor's vein, and then the remaining saline is discarded. The most prominent veins on the arms of the donor and the recipient are selected; usually these are superficial veins on the ventral surface of the arm over the elbow joint, but frequently other veins of the forearm and occasionally the radial veins are preferable. In the case of the donor, a deeper seated, well anchored vein is to be preferred to the easily movable, readily collapsed, superficial vein.

Needles are inserted "toward the heart" because it is easier to introduce needles placed in this direction. The slight advantage in placing the donor's needle "toward the hand" does not compensate for the added difficulties encountered.

The skin is pierced beside the vein first, and then the vein is entered with a separate, slow, purposeful movement. Do not "peck" or "jab" at a vein. It is best to have about two thirds of the length of the needle buried beneath the skin.

Needles must be sharpened before each transfusion. This is imperative. Fairly long concave bevels are best. We "hollow-grind" our needles by use of a small motor-driven emery wheel which is supplied at small cost by all firms that sell laboratory supplies. A 15 gage needle is used for the recipient and a 13 gage needle for the donor. The rubber tubing should have thick, stiff walls, cut in 9 inch lengths and a lumen that is just large enough to admit the adaptors.

When the needles are in position, the donor's syringe is first filled with blood from the donor; then the stopcock is reversed, and this blood is emptied into the recipient's circulation while the assistant fills his syringe with donor's blood. This procedure is repeated until a sufficient amount has been transferred.

In the majority of transfusions, 500 cc. can be given with the same two syringes. Occasionally, they begin to stick before the transfusion is completed, and it is necessary to exchange them for fresh ones; more than one change is rarely necessary. No less than four syringes should constitute a set. A slight amount of "sticking" is sometimes encountered which lasts while two or three syringefuls are being taken, and which is eliminated if additional strength is exerted when the plunger is pulled or pushed.

Ether or any other substance should not be used to prevent "sticking" of the plungers. Speed in filling and emptying syringes is important for the success of the transfusion.

When the transfusion is finished, the operator should clean the apparatus. It should be placed in the cover, rolled up and sterilized in the autoclave immediately at 5 pounds' pressure for ten minutes. A convenient method is to autoclave the set under the same conditions observed for rubber gloves. Thus a sterile apparatus is always ready. A lubricant or coating should not be used for any part of the apparatus, and a new rubber tubing should be used for each transfusion.

The apparatus can be used satisfactorily by one person if an assistant is not available. In that case the assistant's syringe is left in position but is disregarded when the transfusion has been started. Of course, an assistant is desirable to provide a steady flow of blood.

2201 Jefferson Avenue East

STUDIES IN INTESTINAL OBSTRUCTION

II. THE ABSORPTION OF HISTAMINE FROM THE OBSTRUCTED BOWEL *

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In intestinal obstruction, the factor of absorption from the bowel is uniformly acknowledged as being of the greatest importance. It is generally stated that with the stretching and damaging of the wall of the bowel incident to distention by obstruction, absorption of the toxic material from the bowel occurs to which the mucous membrane of the normal bowel is impermeable.

It has been adequately demonstrated that the obstructed bowel permits the absorption of substances from its lumen to which the normal bowel is permeable. Braun and Borrutau [1] have been able to show that strychnine is absorbed from the obstructed intestine of the dog, but at a slower rate than from the normal intestine. Clairmont and Ranzi [2] found that potassium iodide was absorbed from the obstructed intestine of the dog more rapidly during the first ten hours following the obstruction than from the normal bowel. From ten to fifteen hours after the obstruction, the absorption became reduced in amount and quickly sank to a low level. Enderlen and Hotz [3] observed that the absorption of various concentrations of saline and dextrose in the obstructed intestine of the dog was retarded from the start; some time following the establishment of the obstruction, the absorption from the obstructed bowel was slight. Later during obstruction they observed an exudation of fluid into the bowel. Enderlen and Hotz [3] stated that in the animal with intestinal obstruction, the absorption from the nonobstructed segments is also diminished. In contrast to the greatly changed external appearance of the bowel in strangulation obstruction, Enderlen and Hotz found that there was little change from the normal bowel in the absorption of varying con-

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* From the Departments of Surgery and Physiology of the University of Minnesota.

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1. Braun, W., and Borrutau, H.: Experimental kritische Untersuchungen ueber den Ileus Tod, Deutsche Ztschr. f. Chir. **96**:544, 1908.

2. Clairmont P., and Ranzi, E.: Zur Frage der Autointoxication bei Ileus, Arch f. klin. Chir. **73**: 696, 1904.

3. Enderlen and Hotz: Ueber die Resorption bei Ileus and Peritonitis, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:755, 1911.

centrations of dextrose and saline. Braeye,[4] in studying the passage of toxins obtained from an obstructed bowel through an isolated obstructed loop, was unable to determine any abnormal absorption with soap solution.

The nature of the toxin in intestinal obstruction is a disputed point even among those who generally accept the absorption of an intestinal toxin as the cause of death. Every one agrees, however, that if there is a toxin in the bowel of the animal in which intestinal obstruction has been produced which is not present in the intestine of the normal animal, the toxin has its source above the point of obstruction and probably takes origin in protein disintegration.

In this study, histamine was placed in the intestine of both the normal dog and the dog with intestinal obstruction, and acute experiments were performed to test for the physiologic action of histamine as observed in the blood pressure. Gerard [5] stated that the toxic substance in intestinal obstruction actually is histamine. It is known, however, that histamine is present in the bowel of both man and the normal dog [6] and also in the bowel of the dog with intestinal obstruction.[7] The eliciting of the physiologic test for histamine when injected into the bowel of the dog with intestinal obstruction would adduce convincing proof that the bowel of the animal was permeable to toxic substances which the normal bowel did not allow to pass.

METHOD

Blood pressure tracings were recorded by a kymograph from the carotid artery of the dog under ether anesthesia. After the pressure level had been established, the abdomen was opened, and the pressure level was again allowed to adjust itself following the transitory change that occasionally occurred when the abdomen was opened or a loop of bowel was raised. Histamine dichloride was then injected into the

4. Braeye, Louis: Contribution to the Study of Toxic Absorption from the Intestinal Tract in Experimental High Obstruction, Bull. Johns Hopkins Hosp. **40**: 33, 1927.

5. Gerard, R. W.: Chemical Studies on Intestinal Intoxication; The Presence and Significance of Histamine in an Obstructed Bowel, J. Biol. Chem. **52**: 116, 1922; The Lethal Agent in Acute Intestinal Obstruction, J. A. M. A. **79**: 1581 (Nov. 4) 1922.

6. Hanke, M. T., and Koessler, K. K.: Studies on Proteinogenous Amines; On the Presence of Histamine in the Mammalian Organism, J. Biol. Chem. **59**:879, 1924. Meakins, J., and Harington, C. R: The Relation of Histamine to Intestinal Intoxication; I. The Presence of Histamine in the Human Intestine, J. Pharmacol. & Exper. Therap. **18**:455, 1921. Mellanby: An Experimental Investigation on Diarrhea and Vomiting of Children, Quart. J. Med. **9**:165, 1916.

7. Gerard, R. W. (footnote 5, second reference).

lumen of the bowel with a fine hypodermic needle. This procedure was first carried out in the normal, and then in the obstructed ileum and duodenum. Blood pressure tracings were also obtained in a few dogs in which duodenal obstruction had been created two days previously without injecting histamine into the obstructed bowel at the time the observations on the blood pressure were made. A number of tracings were made on dogs in which strangulation obstruction had been established a few hours previously. In some of these experiments, histamine was injected into the bowel before the strangulating mechanism was released; in others, the introduction of histamine into the bowel was omitted.

In a few of the early experiments the tracings were made under a combination of morphine and local anesthesia, and the pressure was obtained from the femoral artery. In most of the tracings, however, ether anesthesia was employed, and the pressure was recorded from the carotid artery. Unless otherwise specified, it is implied that the blood pressure was registered from the carotid artery and that ether anesthesia was used. Whenever the intestines were obstructed by operation quite an interval prior to the time that the tracing was made, aseptic technic was employed, and the animals were allowed to recover from the anesthetic before the second procedure was begun. Severed gut obstructions were established by cutting across the bowel and inverting the ends. Strangulation obstructions were created by placing a gauze ligature around a loop of bowel, from 3 to 5 feet (91.44 to 152.4 cm.) in length, together with its mesentery. The degree of constriction obtained by the ligature was varied. In a few instances in which complete cessation of blood flow was desired, Carmalt noncrushing clamps were placed across the mesentery. In this study, pressure readings were made on twenty-eight dogs.

EXPERIMENTS

EXPERIMENT 1 (dog 71).—Nov. 27, 1926: Absorption of histamine from the normal duodenum.

A tracing was made on a large female collie with a cannula in the right femoral artery under ether anesthesia at 12:40 p. m. The blood pressure at the beginning of the tracing was 124 mm. of mercury. The abdomen was opened and the duodenum isolated by clamping off a segment about 8 inches (20.3 cm.) in length with intestinal clamps cross the bowel. At 1:10, 10 mg. of histamine was injected into the femoral vein with only a slightly perceptible change in the arterial pressure. At 1:20, 10 mg. of histamine was injected into a mesenteric vein with an immediate depression of the pressure to 75 mm. of mercury. At 1:40, the blood pressure had risen to 90 mm. of mercury. Ten milligrams of histamine was then injected into the femoral vein with a drop in pressure to 50 mm. of mercury. After twenty minutes, the pressure rose to 90 mm. of mercury, and 50 mg. of histamine and enough water to make the obstructed loop of the intestine tense, was injected into it. Change in the

blood pressure did not occur over a half hour period. Ten milligrams of histamine was then injected into a mesenteric vein with an immediate reduction of pressure to 44 mm.; death resulted.

Summary.—A physiologic effect was obtained when histamine was injected intravenously into the systemic and into the mesenteric veins. The injection of 50 mg. of histamine into the duodenal loop which had been made tense by distending it with water did not have any effect.

EXPERIMENT 2 (dog 79).—Dec. 20, 1926: Absorption of histamine from the normal ileum.

A tracing was started at 10:17 a. m. (fig. 1). The arterial pressure was 140 mm. At 10:34, the abdomen was opened, the pressure being 150 mm. At 10:48, rubber covered clamps were applied 3 feet apart across the lower part of the ileum. At 10:55, the pressure was 130 mm. At 10:57, 50 mg. of histamine and enough water to make the loop distended was injected into the intestine with a fine hypodermic needle. At 11:07, the arterial pressure was 128 mm. The pressure continued at the same level. At 12:04 p. m., one hour and nine minutes following the injection of the histamine into the lower ileal loop, the pressure was still unchanged. Ten milligrams of histamine was then injected into a mesenteric vein with an immediate fall of pressure to 70 mm. At 12:09, 1 cc. was aspirated from the loop into which the histamine had been injected, with a quick fall in pressure to 56 mm., followed by a progressive decline. The dog was killed with ether.

Summary.—A fall in pressure did not occur after one hour and nine minutes following the injection of 50 mg. of histamine into the normal loop of the ileum.

EXPERIMENT 3 (dog 80).—Dec. 20, 1926: Aseptic gut obstruction (lower part of the ileum) was established at 11 a. m.

A tracing was started December 21, at 3:06 p. m. The arterial pressure was 110 mm. of mercury. The abdomen was opened at 3:12, and six minutes later the arterial pressure was 136 mm. A rubber covered clamp was applied across the bowel about 18 inches (45.7 cm.) proximal to the obstruction in the ileum. The blood pressure at 3:25 was 130 mm. of mercury. At 3:26, 50 mg. of histamine was injected into the obstructed loop. At 3:32, the blood pressure was the same. At 3:45, 3:54 and 4:07, the systolic pressure was 130 mm. At 4:17 the blood pressure was 124 mm. of mercury. At 4:30, the blood pressure dropped to 118 mm. of mercury, and 25 mg. more of histamine was injected into the obstructed loop. At 4:45, the blood pressure was 110 mg.; at 4:57, it remained the same. Three cubic centimeters of contents from the obstructed loop containing histamine was then injected into a mesenteric vein with an immediate fall in pressure to 56 mm. At 5:03, the blood pressure had gradually returned to 80 mm. Three cubic centimeters of intestinal contents was then aspirated from the colon and injected without effect. At 5:15, the blood pressure was 70 mm. of mercury. Three cubic centimeters were aspirated from the obstructed loop containing histamine and injected into a mesenteric vein with a fall to 40 mm. of mercury. Air was injected into the heart; death resulted.

Summary.—A fall in pressure did not occur in one hour in the dog with severed ileal gut obstruction of twenty-four hours' duration after 50 mg. of histamine was placed in the bowel.

EXPERIMENT 4 (dog 72).—Nov. 30, 1926: Aseptic severed duodenal gut obstruction was established at 11 a. m.

On December 1, at 11:55 a. m., a tracing was started under procaine hydrochloride anesthesia from the right femoral vein of the abdominal wall after a

previous subcutaneous injection of 240 mg. of morphine sulphate; pressure at this time was 154 mm. of mercury. At 11:58, the abdomen was opened. The pressure remained unchanged. At 12:00, 100 mg. of histamine was injected into the obstructed duodenal loop. A rubber covered intestinal clamp was applied across the gut at the pylorus. At 12:15 p. m., the pressure was still 154 mm. of mercury. At 12:17, a clot was removed from the vessel, following which there was a fall in pressure to 120 mm. of mercury. At 12:22, another clot was removed from the vessel, the pressure, meanwhile, having fallen to 80 mm. of mercury. At 12:32, the histamine was removed from the bowel by aspiration, without any change in pressure. At 12:47, one fourth of the material removed

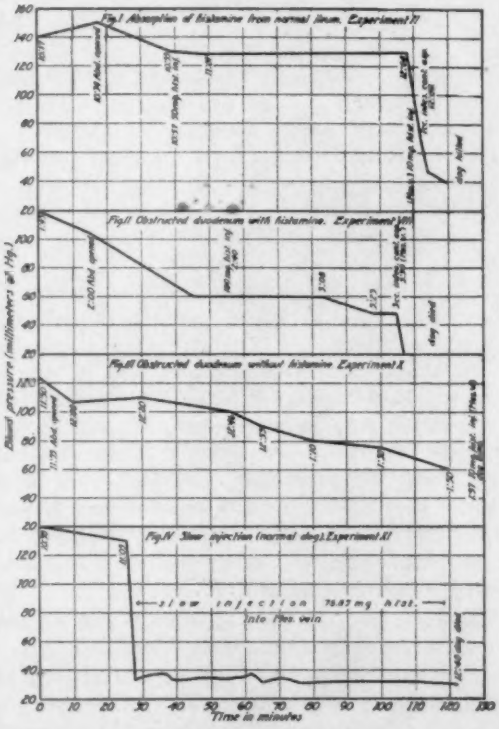
Fig.I Absorption of histamine from normal ileum. Experiment 7
Fig.II Obstructed duodenum with histamine. Experiment 8
Fig.III Obstructed duodenum without histamine Experiment 10
Fig.IV Slow injection (normal dog) Experiment 11
slow injection 7.5 mg hist.
into fem. vein
Blood pressure (millimeters of Hg.)
Time in minutes

Chart 1.—Figure 1, experiment 2, is the blood pressure curve showing that the placing of histamine in the normal ileum did not cause any effect; figure 2, experiment 8, blood pressure tracing showing the effect of placing histamine in the obstructed duodenum; figure 3, experiment 10, blood pressure tracing showing the effect of obstruction without injecting histamine in the bowel, and figure 4, experiment 11, blood pressure tracing showing the effect of extremely slow injection of histamine intravenously.

from the loop was injected into a mesenteric vein, causing an immediate drop in pressure almost to the base line; death followed at 12:58.

Summary.—A gradual fall of pressure occurred after the introduction of 100 mg. of histamine into the duodenal loop of a dog with a two day severed gut duodenal obstruction.

EXPERIMENT 5 (dog 73).—Dec. 2, 1926: Aseptic severed gut duodenal obstruction was established at 10:30 a. m.

At 12:06 p. m., a tracing was started under morphine and procaine hydrochloride anesthesia of the abdominal wall, the dog having thirty minutes previously been injected hypodermically with 140 mg. of morphine. The blood pressure at this time was 140 mm. of mercury. The abdomen was opened at 12:10. At 12:13, 100 mg. of histamine was injected into the obstructed duodenal loop. The blood pressure was 118 mm. of mercury. At 2:25, the blood pressure was unchanged. At 12:38, the anesthesia proved insufficient and ether was administered. At 12:50, 80 mg. of morphine was again given hypodermically in an endeavor to carry on the experiment without ether. At 1 o'clock, the blood pressure was 80 mm. of mercury and the experiment was discontinued because of unsatisfactory anesthesia.

EXPERIMENT 6 (dog 74).—Dec. 6, 1926: Aseptic severed duodenal obstruction was established at 2:30 p. m.

A tracing was started under ether anesthesia (no morphine) on December 7, at 11:40 a. m., pressure being recorded from the right femoral artery. At the beginning of the tracing, the pressure was 120 mm. of mercury. The abdomen was opened at 11:50. The obstructed duodenal loop was raised and an intestinal clamp applied across the pylorus at 11:58. The blood pressure was 120 mm. at 12:06 p. m. At 12:15, a clot was removed from this vessel, and the cannula was transferred to the left femoral artery. The blood pressure was 128 mm. of mercury. At 12:30, another clot formed, and the cannula was removed and placed in the right carotid artery. At 12:45, the blood pressure was 128 mm. of mercury. Three milligrams of histamine mixed with a little of the intestinal contents from a normal loop was then injected into a mesenteric vein; this was followed by an immediate drop in pressure to 30 mm. A gradual rise then followed, which reached 90 mm. of mercury at 1:15. A slow but gradual fall in pressure occurred during the next hour. At 2:10, the blood pressure was 60 mm. of mercury. At 2:22, the arterial pressure had fallen to 40 mm. At this time, 50 mg. of histamine was injected into a normal loop of the ileum, and intestinal clamps were applied across the bowel about a foot apart. A slow fall in pressure continued; death resulted at 2:35.

Summary.—Duodenal obstruction was established and continued for twenty-one hours. The physiologic effect of histamine was noted after the injection of 3 mg. of this drug into the mesenteric vein. Histamine was not placed in the obstructed duodenal segment. The pressure fell gradually from the beginning of the tracing. The injection of 50 mg. into a normal ileal loop did not accelerate the drop.

EXPERIMENT 7 (dog 81).—Dec. 20, 1926: Severed gut obstruction was established in the lower part of the ileum at 11 a. m.

On December 21, the dog was given 300 cc. of a 3 per cent sodium chloride solution subcutaneously; when the tracing was made on December 22, the animal was in relatively good condition. Unfortunately, the tracing was lost; so measurements of the arterial pressure at any given time are not available. The following record of the experiment was written at the time the tracing was made. At 1 p. m., when the tracing was started, the blood pressure was good. The abdomen was opened and the obstructed loop delivered. A rubber covered clamp was applied across the bowel about a foot proximal to the obstruction. One hundred milligrams of histamine was then injected with a fine hypodermic needle into the lumen of the bowel. Fall in pressure was not observed over an interval of one hour and fifteen minutes. At this time, a little of the intestinal contents

from the ileum below the severed obstruction was aspirated and injected into the mesenteric vein without much effect. The same procedure was followed with a little of the contents of the loop proximal to the clamp which had been applied across the bowel. No great effect followed this injection. A few centimeters of the contents was then aspirated from the loop in which the histamine had been placed, and this was injected into a mesenteric vein and resulted in a great fall in pressure and in the death of the animal.

Summary.—A severed gut obstruction was established low in the ileum and maintained for two days. The dog was given saline solution subcutaneously on the day following the obstruction, without a fall in pressure after one hour and fifteen minutes following the introduction of 100 mg. of histamine into the loop of the obstructed bowel.

EXPERIMENT 8 (dog 90).—Jan. 3, 1927: Duodenal obstruction was established in the dog at 3 p. m. A tracing was started on December 5, at 1:45 p. m. (fig. 2). The arterial pressure was 120 mm. The abdomen was opened at 2 o'clock. The blood pressure was 104 mm. At 2:17, the loop was raised. The blood pressure was 98 mm. The duodenal loop was delivered and covered with warm packs of saline solution. A rubber covered clamp was then applied across the duodenum at the pylorus. In the meantime, the blood pressure had fallen to 60 mm. of mercury. At 2:40, 100 mg. of histamine was placed in the obstructed duodenal loop; the blood pressure had been falling gradually from the start. Acceleration was not noted, following this injection of histamine. At 3:08, the blood pressure was 60 mm. and at 3:23, 48 mm. At 3:30, 3 cc. of intestinal contents was aspirated from the obstructed loop and injected into a mesenteric vein with an immediate drop of pressure to 20 mm. At 3:40, the dog was dead.

Summary.—A duodenal severed gut obstruction was maintained for two days. There was a gradual fall in pressure from the start. Acceleration did not occur following an injection of 100 mg. of histamine into the obstructed loop.

EXPERIMENT 9 (dog 95).—Jan. 6, 1927: Aseptic duodenal obstruction was established at 3 p. m. Two days later a tracing was started at 12:50 p. m. The blood pressure was 124 mm. The abdomen was opened at 1 o'clock, and the duodenal loop was delivered at 1:10. One hundred milligrams of histamine was injected into the obstructed bowel at 1:20. The blood pressure was 130 mm. of mercury at 1:30. At 1:40, 108 mm.; at 1:45, 90 mm., and at 2:10 it remained unchanged. A large portion of the contents of the obstructed loop into which histamine had been injected were then aspirated and injected into a mesenteric vein with an immediate drop in pressure to 50 mm. of mercury. Death occurred at 2:15.

Summary.—A severed gut duodenal obstruction was maintained for two days with a gradual decrease in pressure following an injection of 100 mg. of histamine into the obstructed bowel.

EXPERIMENT 10 (dog 97).—Jan. 10, 1927: Obstruction was established in the dog at 2 p. m. by severing the duodenum and turning in the ends of the bowel just below the pancreatic ducts. A tracing was started on January 12 at 11:50 a. m. (fig. 3). The arterial pressure was 124 mm. The abdomen was opened at 11:55. At 12 o'clock, the arterial pressure was 106 mm. At 12:20, the arterial pressure was 110 mm. of mercury. Histamine was not injected into the bowel in this experiment. The blood pressure was 100 mm. at 12:46; at 12:55, 90 mm.; at 1:10, 80 mm.; at 1:30, 76 mm., and at 1:50, 60 mm. At

1:57, 10 mg. of histamine was injected into a mesenteric vein; this was followed by irregular respirations and death occurred in three minutes.

Summary.—A severed gut duodenal obstruction was maintained for two days. There was a gradual fall in pressure from the time the abdomen was opened and the tracing started. Histamine was not placed into the bowel. Ten milligrams of histamine injected into the mesenteric vein killed this dog in two hours and two minutes after the abdomen was explored.

EXPERIMENT 11 (dog 142).—March 30, 1927: Histamine was slowly injected into the mesenteric vein of a normal dog by a dripping mechanism so that the rate of the flow could be accurately determined (fig. 4). One hundred milligrams of histamine was placed in 100 cc. of water. The rate of the flow was so gaged that 100 cc. would run in in one hundred and twenty minutes (two hours). At the end of sixty minutes, 50 cc. had been injected. The tracing of the pressure was started at 10:38 a. m. A slow injection was begun at 11:05. Immediately there was a marked reduction in pressure. The pressure was sustained at this low level till death at 12:40 p. m. when 76.85 mg. of histamine had been injected at the rate of 0.83 mg. per minute. At the beginning of the experiment, the pressure was 140 mm.; after opening the abdomen, 120 mm., and when slow injection was started, 130 mm. A few seconds after injection was begun, the pressure fell to 30 mm. Occasionally it rose to 40 or 50 mm., but it continued at low level till death.

Summary.—Eighty-three hundredths milligrams of histamine was injected into a mesenteric vein of a normal dog per minute. The pressure fell at once to a low level and was sustained by a continuous slow injection. Ninety-five minutes later, when 76.85 mg. of histamine had been injected, death occurred.

EXPERIMENT 12 (dog 143).—April 1, 1927: A slow injection of histamine was made into a mesenteric vein of a dog in which intestinal obstruction had been established two days previously (duodenal obstruction). A tracing was started at 9:35 a. m. (fig. 5). The abdomen was opened at 9:50. Slow injection was begun at 10:06. At 12:07 p. m., 100 mg., had been injected. Death occurred at 12:17. At the beginning of the experiment the pressure was 140 mm. After opening the abdomen, the pressure was 135 mm., and at 10:06, when the injection of histamine was begun, 130 mm. There was a sudden drop to 80 mm. about a minute after slow injection was started. In a few minutes, the pressure rose to 94 mm. One hour after slow injection had been started, the pressure fell to 65 mm. When 100 mg. had been injected by this method at 12:07 p. m., the pressure was 60 mm. Death occurred at 12:17.

Summary.—Histamine was slowly injected into the mesenteric vein of a dog with a duodenal obstruction of two days. A gradual decline occurred after a sharp initial fall in the arterial pressure.

EXPERIMENT 13 (dog 144).—April 22, 1927: (1) Absorption of histamine from the normal bowel under a measured pressure of 80 mm.; (2) interrupted slow injection of histamine into a mesenteric vein. A tracing was started at 10:55 a. m. at a pressure of 140 mm. (fig. 6). The abdomen was opened at 11:02 a. m.; the pressure was 130 mm. Following the opening of the abdomen, the pressure fell to 90 mm. At 11:10 a. m., the pressure had risen to 100 mm., and rubber covered clamps were applied across the bowel to a segment of the upper part of the jejunum about 2 feet (60.9 cm.) in length. One hundred milligrams of histamine was injected into the segment of the bowel, and a measured water pressure of 80 mg. of mercury was established in the segment. The pressure rose to 110 mg. of mercury at 11:20 a. m. When the pressure was discontinued at 12:10

p. m., one hour after the histamine had been injected, the pressure was 120 mm. of mercury. Interrupted slow injection of histamine into the mesenteric vein was then begun two minutes later. At this time, after 8.33 mg. of histamine had been injected, the systolic pressure fell to 60 mm. The slow injection was then discontinued, and in ten minutes the arterial pressure had risen to 100 mm. The slow injection was started again, and in ten minutes the pressure had fallen to 44 mm. of mercury. The injection was again discontinued, and after ten minutes the pressure was 100 mm.

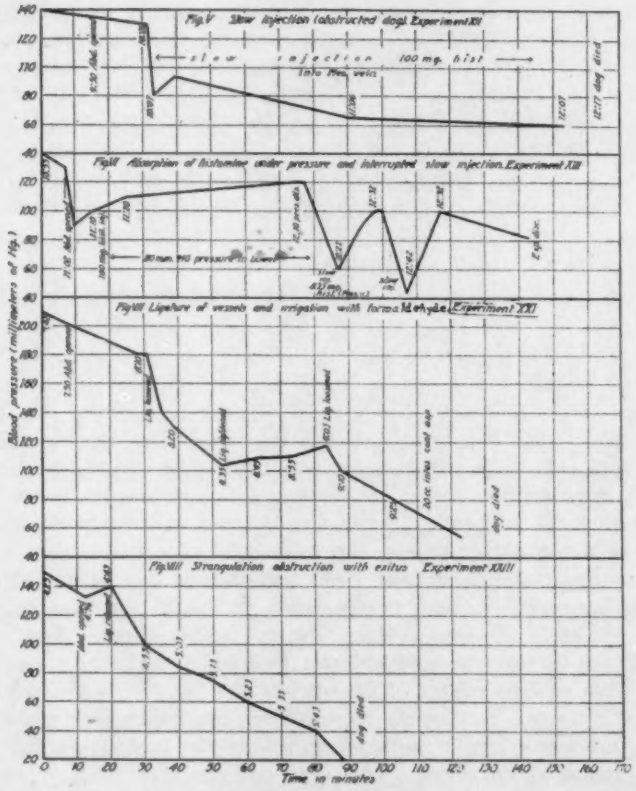
Fig V Slow injection (obstructed dog) Experiment XII
slow injection 100 mg. hist
into mes. vein
Fig VI Absorption of histamine under pressure and interrupted slow injection. Experiment XIII
Fig VII Ligature of vessels and irrigation with formaldehyde Experiment XXI
Fig VIII Strangulation obstruction with exitus Experiment XXIII
Blood pressure (millimeters of Hg.)
Time in minutes

Chart 2.—Figure 5, experiment 12 is a blood pressure tracing showing the effect of the slow intravenous injection of histamine in an obstructed dog; figure 6, experiment 13, blood pressure tracing showing the effects of the absorption of histamine placed in the bowel under pressure, and subsequent, slow, interrupted injection of histamine in the mesenteric vein; figure 7, experiment 21, blood pressure tracing showing the effect of ligation of vessels followed by irrigation of the bowels with formaldehyde, and figure 8, experiment 23, blood pressure tracing showing the effect of releasing the ligature which caused the strangulated obstruction.

Summary.—1. One hour after 100 mg. of histamine had been placed in a segment of the normal bowel under a sustained pressure of 80 mm. of mercury, there was no fall in pressure. 2. On interruption of the slow injection of histamine into the mesenteric vein, the blood pressure recovered and fell again when the injection was resumed.

EXPERIMENT 14 (dog 84).—Dec. 23, 1926: Aseptic strangulated gut obstruction was established at 11:30 a. m. by tying a gauze ligature around 4 feet of the ileum and mesentery just snugly enough so that pulsations in the vessels beyond the ligature were not arrested. The dog was allowed to recover from the anesthesia. A tracing was started at 1:55 p. m. The arterial pressure was 80 mm. of mercury. The abdomen was opened at 2:01 p. m. at which time the blood pressure was 60 mm. At 2:13 p. m. it was 60 mm. of mercury. Seventy-five milligrams of histamine was injected into the strangulated loop which was already discolored. The blood pressure had dropped to 40 mm. of mercury at 2:30 p. m. At 2:36, the constriction about the intestine and mesentery was released, and the pressure gradually declined to 30 mm. of mercury. At 3:32 p. m. a few cubic centimeters of the intestinal contents were aspirated from the strangulated loop and injected into a mesenteric vein. Death resulted at 3:40 p. m.

Summary.—Venous strangulation obstruction was established for two and one-half hours. The blood pressure was low at the start, with a gradual decline. Seventy-five milligrams of histamine was placed in the strangulated loop. In thirty-five minutes after the abdomen was opened, the pressure had fallen from 80 to 40 mm. of mercury. Constriction about the bowel and the mesentery was then released, with an accelerated fall in pressure.

EXPERIMENT 15 (dog 85).—Dec. 27, 1926: Strangulation of the loop was established at the time of operation. A tracing was started at 11:10. The arterial pressure was 170 mm. of mercury. The abdomen was opened at 11:17. A loop of the ileum about 4 feet in length was delivered at 11:22. A ligature was tightly placed about the bowel at 11:28, the pressure at this time being 160 mm. At 11:48 the pressure was still the same. The ligature was loosened a little with a just perceptible fall in pressure. At 12 o'clock, the ligature was loosened a little further, with a more definite fall in pressure in two or three minutes. At 12:07 p. m., the pressure had dropped to 110 mm. of mercury and the ligature was removed with a rather sharp decline in pressure. At 12:14 the pressure had fallen to 80 mm., and the ligature was again tightened. At 12:30, the pressure had risen to 130 mm. At 12:34, the ligature was again loosened, and at 12:45, the pressure had fallen to 118 mm. The ligature on the bowel was alternately tightened and loosened three more times with less reaction following each release of the constriction, but with a gradual decline of the arterial pressure. During the time that the constriction was maintained, the blood pressure was definitely sustained with little rise in pressure, but with each release a gradual fall occurred. The blood pressure at 1:30 p. m. was 90 mm. At 1:45, 50 mg. of histamine was injected into the bowel without an additional fall. At 2:20, the pressure was 64 mm. A few cubic centimeters was aspirated from the strangulated loop into which the histamine had been injected. Death occurred at 2:30 p. m.

Summary.—Strangulation obstruction was established at the time the tracing was made. Twenty minutes later, the constriction was released, accompanied by a fall in pressure. When the ligature was tightened, the pressure rose. Two hours later, histamine was placed in the strangulated loop without an additional fall being noted.

EXPERIMENT 16 (dog 86).—Dec. 28, 1927: Strangulation obstruction was established. A tracing was started at 10:50 a. m. The blood pressure was 170 mm. The abdomen was opened at 10:57 without any change in the blood pressure. At 11:20, a loop of the ileum 3 feet in length was strangulated, together with its

mesentery, by being constricted tightly with a gauze tie. At 11:42, the ligature was loosened without causing a definite change in the arterial pressure. At 11:55, the loop was again constricted and loosened at 12:20 p. m. with a gradual but definite fall of pressure to 140 mm. At 12:42, the ligature was tightened again and loosened at 1:16; following this, there was a slight and gradual fall of pressure to 120 mm. When the loop was constricted again at 1:30, the pressure continued to fall slowly. At 1:45, the pressure was 100 mm. The loop was untied at 1:50 without much effect. At 2:05 p. m., 10 mg. of histamine was injected with an immediate depression of pressure to 40 mm. of mercury; death followed.

Summary.—Strangulation obstruction was established at operation. Twenty-two minutes later, the constriction was released without a fall in pressure. The ligature was tightened again and loosened after twenty-five minutes, with a definite fall in pressure. An injection of only 10 mg. of histamine into a mesenteric vein killed this dog after the ligature had been alternately tightened and loosened over a period of two hours and forty-five minutes.

EXPERIMENT 17 (dog 87).—Dec. 28, 1926: Strangulation obstruction was established. A tracing was started at 2:35 p. m., the arterial pressure being 180 mm. of mercury. The abdomen was opened at 2:40. At 2:55, the blood pressure was 144 mm. At 3:00, the loop of the ileum and its mesentery, about 3 feet in length, were ligated with a gauze tie. At 3:25, the arterial pressure was 164 mm. At 3:30, the constriction about the bowel and the mesentery was released without causing any change. The blood pressure was 160 mm. of mercury. At 3:40 another loop of the ileum near the cecum, also about 3 feet in length, and its mesentery, were constricted with a gauze tie. The ligature was released at 4 o'clock, and a slow fall in pressure to 120 mm. occurred. At 4:35 the loop was again constricted. The blood pressure was 130 mm. of mercury at 4:55. At 5, the ligature was loosened; this was followed by a slow fall of pressure to 118 mm. At 5:05, 5 cc. of intestinal contents was aspirated from this loop and injected into a mesenteric vein, causing a fall in blood pressure to 78 mm. At 5:15, another such injection was made. The dog died at 5:30.

Summary.—Repeated constriction and release of strangulation was accompanied by a slow but gradual fall of arterial pressure.

EXPERIMENT 18 (dog 88).—Dec. 29, 1926: Strangulated obstruction of about 5 feet (152 cm.) of midileum was established at 11:40 a. m. by placing a tight gauze tie about the bowel and the mesentery under aseptic technic. The dog was allowed to recover from the anesthesia. A tracing was started at 1:45 p. m. under ether anesthesia. The blood pressure was 176 mm. of mercury. The abdomen was opened at 1:50 and a slight but sharp fall in pressure followed. At 1:55 the pressure was 144 mm.; at 2 it had risen to 160 mm. At 2:05, the strangulated loop was delivered with a shap fall to 124 mm. of mercury. At 2:10, the blood pressure had risen to 150 mm. The bowel was a blackish-blue and indurated to touch. The ligature constricting the bowel and the mesentery was loosened with an almost immediate fall in blood pressure to 110 mm. of mercury. At 2:20, the ether anesthesia was light; a short convulsive seizure occurred, during which the blood pressure rose to 130 mm. of mercury; this was followed by a sharp decline to 84 mm. of mercury, above which the pressure never rose again. At 2:35, the arterial pressure was 80 mm. and at 2:40, the systolic pressure was 40 mm. At 2:47, the blood pressure was 56 mm.; at 3 and at 3:09, 62 mm. The ligature was again tightened about the loop; this was followed by a slight but transient rise in pressure at 3:15 to 76 mm.

of mercury and then by a gradual decline to 50 mm. at 3:30. The ligature was again loosened, and the pressure continued to fall. At 3:35 the pressure was 30 mm. Seven cubic centimeters of intestinal contents was now aspirated from the strangulated loop and injected into a mesenteric vein with a gradual decrease of pressure. The dog died at 3:50.

Summary.—Strangulated obstruction of two hours' duration was established. A marked fall in pressure occurred when the constriction was released. When the ligature was tightened, a short rise in pressure occurred.

EXPERIMENT 19 (dog 89).—Dec. 30, 1926: Strangulated obstruction of a loop of the lower part of the ileum, together with its mesentery was performed under aseptic technic at 11:30 a. m. A carotid artery tracing was started at 2 p. m. under ether anesthesia. The tracing from this experiment has also been lost, so that only the protocol written at the time is available; consequently, definite figures as to arterial pressure at any time cannot be given. At the beginning of this experiment, the pressure was good. At 2:05, the abdomen was opened without much effect on the pressure. The bowel was only moderately cyanotic and rather thickened on palpation. At 2:20, the ligature about the bowel and mesentery was loosened, with an immediate fall in pressure. At 2:35, the ligature was tightened, and the pressure rose gradually. At 2:50, the ligature was loosened again, and a slight but definite fall in the arterial pressure occurred. Fifty milligrams of histamine was injected into the strangulated bowel at this time, apparently without direct effect on the pressure. At 3:10, a portion of the contents into which the histamine had been injected was aspirated from the loop and injected into a mesenteric vein, causing a great fall in pressure.

Summary.—A strangulated obstruction was established for two and one-half hours. Release of the constriction was attended by a fall in pressure. On tightening the ligature, the pressure rose.

EXPERIMENT 20 (dog 90A).—Dec. 31, 1926: Aseptic strangulated gut obstruction was produced at 11:30 a. m. by tying off a loop of the ileum and mesentery about 5 feet (152.4 cm.) in length. The bowel was then irrigated with a solution of 10 per cent formaldehyde, ether and alcohol until the contents returned clear. The dog was again anesthetized. A tracing was started at 2:50 p. m. The dog was extremely ill. The blood pressure at the beginning of the experiment was 118 mm. of mercury, but fell gradually. At 2:58, the abdomen was opened. The arterial pressure went down to 90 mm. of mercury. The strangulated loop was raised. The blood pressure at 3:10 was 50 mm. and at 3:15, 48 mm. The ligature was detached from the bowel and mesentery. The blood pressure continued to fall at the same rate, and at 3:25 had dropped to 40 mm. At 4, 10 mg. of histamine was injected into a mesenteric vein; death followed.

Summary.—Strangulation obstruction of the intestine was established and maintained for three and one-half hours. The pressure was low at the beginning of the experiment. The dog was in a state of shock. Release of ligature was accompanied by a continued decline in pressure.

EXPERIMENT 21 (dog 92).—Dec. 3, 1927: Strangulated obstruction of 5 feet of the bowel was established at 5 p. m. by tying off the bowel loop and mesentery with a gauze tie under aseptic technic. The bowel was irrigated with 10 per cent formaldehyde, ether and alcohol until the contents returned clear. The dog was anesthetized again with ether at 7:30. A tracing was begun at 7:42, the pressure being 210 mm. of mercury (fig. 7). The abdomen was opened at 7:50. The

arterial pressure was 200 mm. The strangulated loop was moderately cyanotic and discolored with some free hemorrhagic fluid present in the peritoneal cavity. The strangulated loop was carefully delivered and isolated in warm saline packs placed on the abdominal wall. At 8:10 the pressure was 180 mm. of mercury. The ligature about the bowel and the mesentery was loosened at 8:13, with an almost immediate fall in pressure to 140 mm. The vessels to the strangulated bowel were soon pulsating, and at 8:20, the normal luster had returned to the strangulated loop, and the pressure was 132 mm. of mercury. At 8:35, the pressure had fallen to 104 mm. The ligature on the intestine was tightened again. Ten minutes later, at 8:45, the bowel was again moderately cyanotic. The pressure had risen to 110 mm. At 8:55, the pressure remained unchanged; at 9:05, the pressure had arisen to 118 mm., and the constriction on the bowel and the mesentery was loosened again. At 9:10, the color had returned to the bowel, and the vessels were pulsating. The pressure had fallen to 100 mm., and at 9:25 had dropped to 80 mm. Twenty cubic centimeters of intestinal contents was then aspirated from a normal loop, diluted with a little saline solution and injected into a mesenteric vein. The arterial pressure had continued to fall and was then 54 mm. Ten minutes later, the dog was dead.

Summary.—A strangulated obstruction was established and had been maintained for three and one-half hours. The pressure was good when the tracing was started. A release of the constriction was attended by a sudden primary and gradual reduction of pressure. When the ligature was tightened the pressure rose.

EXPERIMENT 22 (dog 140).—March 8, 1927: A large collie was used in this experiment. The tracing was started at 10:40 a. m. The blood pressure was 200 mm. of mercury. The abdomen was opened at 10:50. At 10:55, the mesentery to a loop of the midileum, about 3 feet in length, was clamped off with two Carmalt hemostatic forceps so as completely to deprive this segment of its blood supply. At 12:20, one hour and twenty-five minutes later, the two clamps were released without any alteration in pressure. At 1:25, the blood pressure was unchanged. Air was injected into the left ventricle; death resulted.

Summary.—Strangulation of a loop of the intestine was established at the time of operation. Release of the ligature one hour and twenty-five minutes later did not show a fall in pressure.

EXPERIMENT 23 (dog 145).—April 13, 1927: A loop of the intestine was strangulated for 30 inches (76.2 cm.) by placing clamps on the mesentery at 10:30 a. m. A tracing was started at 4:23 p. m. under ether anesthesia; the clamps were removed at 4:43 (fig. 8). The bowel was markedly discolored. From the time the clamps were loosened, the pressure gradually fell. About twenty-five minutes after loosening the clamps, the bowel was regaining luster, but the blood pressure continued to decrease, and the dog died at 5:53, one hour and ten minutes after the removal of the clamps. The pressure at the beginning of the tracing was 150 mm.; at 4:36, just after opening the abdomen, 132 mm.; at 4:43, when the clamp was loosened, 140 mm.; ten minutes after loosening the clamp, 100 mm.; at 5:03, 84 mm.; at 5:13, 75 mm.; at 5:23, 60 mm.; at 5:33, 50 mm.; at 5:43, 40 mm., and at 5:50, 20 mm. Death occurred at 5:53.

Summary.—A strangulation obstruction was established and maintained for six hours. The pressure was good at the beginning of the experiment. After the clamps were released, there was a gradual reduction in pressure followed by death in one hour and ten minutes.

EXPERIMENT 24 (dog 146).—April 16, 1927: Strangulation obstruction of the intestine was established at 10:30 a. m. by ligating 4 feet of the midileum. A

tracing was started at 1:48 p. m. The blood pressure was 160 mm. of mercury. The abdomen was opened at 1:50 and the ligated loop was found to be very dark. The strangulated loop was opened near one end, and as much of the material in the lumen as possible was pressed out; following this, the loop was irrigated with water until the contents, although slightly hemorrhagic in appearance, returned fairly clear. The blood pressure was 160 mm. of mercury. At 2:02, the obstructing mechanism was released, and the pressure promptly fell to 130 mm. of mercury. At 2:05, the luster was returning to the bowel, and the vessels were pulsating. The pressure had fallen to 108 mm. of mercury. Following this, there was a gradual rise to 130 mm. of mercury at 2:10, with a fall at 2:12 to 98 mm. of mercury. At 2:15, the blood pressure had risen to 130 mm. of mercury, and was apparently sustaining itself at this level. The contents that had previously been aspirated were replaced in the bowel at 2:20 without any effect on the pressure. At 2:22, the blood pressure was 124 mm. of mercury. At 2:24, 15 mm. of histamine was injected into the bowel without apparent effect. The constricting mechanism at this time was tightened, and the blood pressure rose at 2:45 to 140 mm. of mercury. At 2:49, the constricting mechanism was released, and the pressure promptly fell to 110 mm. of mercury. At 2:55, some of the contents were aspirated from the strangulated loop and injected into the mesenteric vein; this was followed by a prompt fall in pressure to 50 mm. of mercury; death then occurred.

Summary.—A strangulation obstruction of the gut was established and maintained for three and one-half hours. Release of the constriction was accompanied by a sharp and definite fall of arterial pressure, even after the contents of the obstructed bowel were washed out. When the constriction was again placed about the bowel and the mesentery, the pressure rose. Release of the strangulating mechanism was again accompanied by a decided fall in pressure. Neither the replacement of the removed intestinal contents in the bowel nor the injection of 15 mg. of histamine into the strangulated bowel accelerated the fall in pressure.

EXPERIMENT 25 (dog 114).—Feb. 3, 1927: A tracing from the carotid artery was started at 3:40 p. m. under ether anesthesia. The pressure was 230 mm. of mercury. The abdomen was opened at 3:55. At 4:10, 4 cc. of peritoneal fluid from a dog with a strangulated gut obstruction[8] was injected into the mesenteric vein with only a slight and transient fall in arterial pressure. At 4:23 another injection of 4 cc. was made with the same result. At 4:32, 15 cc. was injected with a more definite but transient fall of pressure to 176 mm. of mercury. At 4:50, the blood pressure was 200 mm. Fifteen milligrams of histamine was now injected into a mesenteric vein, resulting in a sudden and sustained fall to 130 mm. At 5:15 death was produced by asphyxia.

Summary.—A slight and transient fall of pressure occurred after the injection of peritoneal fluid from an autolyzed loop of the intestine into the mesenteric vein of the dog. Sustained reduction was produced by the injection of 15 mg. of histamine into the mesenteric vein.

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8. The origin of the fluid is as follows: A piece of midileum about 12 inches (30.48 cm.) in length weighing 73 Gm. was removed from one dog and placed in the peritoneal cavity of another after the bowel was irrigated until the contents returned clear. This segment of the bowel was then opened along the antimesenteric border, and the mucosa was washed and scrubbed. When the dog into the peritoneal cavity of which this loop was placed died, two days later, this hemorrhagic fluid was obtained for injection.

EXPERIMENT 26 (dog 133).—Feb. 21, 1927: An aseptic ligation of the aorta and vena cava was performed above the bifurcation with gauze at 12:45 p.m.; two ileolumbar vessels on each side were also ligated to diminish peripheral inosculation. When the dog was anesthetized again, he could not stand up, owing to the anemia and consequent paralysis of the hind extremities. A tracing was started at 3:30 p.m. The blood pressure at this time was 200 mm. of mercury. At 3:45, the ligature was removed from the aorta without effecting a change in pressure. At 3:50, the ligature was removed from the vena cava without any change in the blood pressure for over an hour.

Summary.—A ligation of the aorta and the vena cava was performed. Three hours later, there was no reduction in blood pressure following release of the constriction.

EXPERIMENT 27 (dog 135).—Feb. 28, 1927: At 11:00 a. m., a Carmalt clamp was applied across the splenic pedicle and another across the right renal vessels of a dog. A tracing was begun at 3:20 p.m. with the cannula in the right carotid artery. The blood pressure was 240 mm. of mercury. The abdomen was opened at 3:25, and the spleen was found to be bluish and soft with free hemorrhagic fluid in the peritoneal cavity. At 3:40, the clamp was removed from the splenic vessels. Red spots began to appear on the external surface of the spleen, and the organ became firm in consistency. At 3:55, the blood pressure was 190 mm. of mercury. At 4:05, the clamp was removed from the pedicle of the right kidney without any change in pressure. At 4:25, when the tracing was discontinued, the blood pressure remained at 190 mm. of mercury.

Summary.—A moderate fall in pressure occurred following the release of the clamp on the splenic pedicle which had been placed there more than four hours previously. When the clamp placed on renal pedicle five hours previously was released, a fall in pressure did not occur.

EXPERIMENT 28 (dog 136).—March 5, 1927: A tracing was started at 3:40. The blood pressure was 250 mm. of mercury. At 3:50, 50 mg. of histamine was injected subcutaneously over the wall of the chest. There was a gradual but definite fall of pressure to 200 mm. of mercury at 3:52. At 4 o'clock, the blood pressure had dropped to 170 mm. of mercury. Fifty milligrams more of histamine was injected subcutaneously over the wall of the chest. The blood pressure at 4:01, was 160 mm. of mercury. At 4:05, it had fallen to 150 mm. The pressure was maintained at this level, and the experiment was discontinued.

Summary.—A definite fall of pressure occurred following subcutaneous injection of histamine.

SUMMARY

When from 50 to 100 mg. of histamine was placed in the duodenum or ileum of normal dogs, a fall in pressure was not observed in any of the four animals for a period of an hour or more following the introduction of the drug. The injection of from 3 to 10 mg. of histamine into a mesenteric vein was always followed by a sharp fall in pressure. When a few cubic centimeters of the intestinal contents were aspirated from the loops of the bowel into which histamine had been introduced and were injected into a mesenteric vein, there was a sudden fall in arterial pressure, which characterized the histamine reaction.

In a dog with a severed gut obstruction in the lower part of the ileum of thirty hours' duration, the arterial pressure after the introduction of

first, 50 mg. and then of 25 mg. more of histamine into the bowel was the same as it had been two hours previously when the experiment was begun. In another ileal obstruction of two days' duration, the dog was given 300 cc. of a 3 per cent sodium chloride solution subcutaneously on the intervening day in order to improve his condition for the tracing; no fall in pressure was noted after one hour and fifteen minutes following the introduction of 100 mg. of histamine into the obstructed bowel.

In five dogs, duodenal severed gut obstructions of two days' duration were established before the tracings were made. In three instances, 100 mg. of histamine was placed in the obstructed loop at the time the blood pressure readings were made. In one instance, histamine was not introduced into the bowel. In another dog, 50 mg. of histamine was placed in a normal loop in the ileum. In all five instances, a gradual reduction of blood pressure occurred. This effect was just as striking when histamine was not introduced into the obstructed loop. In two of the three instances in which histamine was placed in the obstructed segment, a great reduction of arterial pressure had occurred before the histamine had been injected into the obstructed bowel. Following the introduction of the histamine, no acceleration of this reduction was observed. It must be remembered that a dog with a duodenal obstruction of forty-eight hours' duration is not a good risk for a blood pressure tracing when the abdomen has been opened under ether anesthesia. These dogs usually survive the obstruction only about seventy-two hours. The gradual decline in pressure observed in these animals is probably thus best accounted for.

Histamine was slowly injected into a mesenteric vein of a normal dog and into a mesenteric vein of a dog with a duodenal severed gut obstruction of two days' duration. Histamine was introduced at the rate of 0.83 mg. a minute. One hundred milligrams of histamine was dissolved in 100 cc. of water, and the rate of the flow was so gaged that 100 mg. would be injected every two hours (min. 120). In both instances, a great and sustained fall of pressure occurred when the injection was begun. In another experiment in which the slow injection method also was practiced, but with interruptions, the same reduction in arterial pressure followed by a recovery on suspending the injection, was noted. When the instillation was resumed, the pressure fell; when discontinued again, a rise of the arterial pressure was observed.

In all of the foregoing tracings made on normal dogs and those with severed gut obstruction, when histamine was introduced into the bowel, the consequence of increasing the pressure in the loop until it was tense by distending it with air and water was tested. No effect was observed. In another instance in which 100 mg. of histamine was placed in a segment of bowel in a normal animal under a measured sustained pressure of 80 mm. of mercury, reduction of the blood pressure had not occurred after an hour's observation.

Tracings were made on eleven dogs in which strangulation obstructions were established by tightly constricting from 3 to 5 feet of the bowel and its mesentery with a gauze tie or by applying Carmalt forceps across the mesentery. In four instances, the strangulation was effected after the tracing was commenced. In the other animals, the strangulation was established aseptically at a period varying from two to six hours before the tracing was begun. Discoloration and thickening of the strangulated segment was noted in all instances. In a few dogs free fluid (hemorrhagic) was present in the peritoneal cavity. In two instances, histamine was injected into the strangulated bowel before the constricting mechanism was released. In the others, the effect on the blood pressure was noted when the ligature was loosened. In two animals with strangulation obstructions, the strangulated loop was irrigated until the contents returned clear at the initial operation. In another instance, the strangulated loop was irrigated until the contents returned clear at the time that the tracing was made, just before the constriction was released.

In every instance in which the strangulation had been established at some time previous to the recording of the blood pressure with a kymograph, a definite and great fall in pressure accompanied the release of the constriction, with a return of the normal luster to the bowel and pulsations in its vessels. This was obtained whether or not histamine had been placed in the bowel prior to the time the ligature was removed. Previous irrigations of the bowel did not obviate the reduction of the pressure when the strangulating mechanism was released. Subsequent injection of histamine into the damaged loop did not appear to accelerate the fall in pressure. When the ligature was reapplied about the strangulated bowel and mesentery, the reduction in pressure usually ceased; the pressure either maintained itself at the previous level, or, what seemed to be more common, exhibited a definite rise. Loosening of the ligature again after an interval of time almost invariably was followed by a decline of the arterial pressure.

In one of the four instances in which the strangulation was established at the time the tracing was made, a fall in pressure was not observed when the strangulation was released. A total anemia of a loop was created in this dog by clamping the mesentery with Carmalt forceps. In two other instances, repeated loosening and tightening of the ligature in these strangulations of shorter duration brought about a slow but gradual reduction of the blood pressure. In one of the animals (dog 15), however, a strangulation of only twenty minutes effected a material reduction in pressure. Fifteen minutes after the release of the constriction, a great reduction occurred. The pressure rose when the constriction was reapplied.

The subcutaneous administration of 50 mg. of histamine brought about a gradual but definite fall in blood pressure in the one dog in which this procedure was carried out. Repetition of the injection occasioned a similar sustained fall of arterial pressure.

The injection into a mesenteric vein of peritoneal fluid from a dog in the peritoneal cavity of which a sterile loop of bowel removed from another dog had been allowed to autolyze, was accompanied by only a slight and transient fall in pressure. When the splenic pedicle was clamped off in another animal, release of the clamp almost five hours later was followed by only a slight and transient fall in the arterial pressure. A release of the constriction applied across the pedicle of the right kidney in the same dog, a few minutes later (more than five hours after the clamp had been placed on the renal vessels) was not attended by a change in pressure. In a dog in which both the aorta and vena cava had been clamped off two and one-half hours previously, change in pressure did not follow the removal of the clamps over a period of an hour. At the time the tracing was started, the dog was unable to stand because of the anemia in the hind quarters.

COMMENT

In these experiments, no evidence was obtained that histamine was absorbed from the normal bowel or from the dog with a severed gut obstruction; at any rate, the physiologic reaction that accompanies intravenous or subcutaneous administration of histamine, was not observed on the introduction of histamine into the bowel. If any absorption of histamine did occur from either the normal or the obstructed bowel, it was not absorbed as histamine. The immediate drop in pressure following the introduction of a few milligrams of histamine into a mesenteric vein demonstrates that the detoxifying influence of the liver is not great for histamine. If histamine was absorbed, it was detoxified in passing through the wall of the bowel. That the histamine did not disappear entirely from the bowel is demonstrated by the fact that aspiration of a few cubic centimeters of the contents of the bowel from the loop into which the histamine had been injected was always attended by a sharp fall in pressure that characterizes histamine action. This fall in pressure was always much greater than when intestinal contents alone were injected.

Hanke and Koessler [6] have been able to show by quantitative chemical tests for histamine that small quantities may be transported to the liver from the intestine in the normal animal. They have found that histamine is present as a normal constituent of the contents of the large intestine in both man and dog. They were able to isolate 5.3 mg. of histamine in 150 mg. of feces from a dog. From the liver of the same animal, 6 mg. of histamine was obtained. They were unable to find

histamine in the intestinal content, the intestinal tract itself and in the livers of two guinea-pigs. They [6] fed 100 mg. of histamine to a normal guinea-pig; no manifestation of illness was apparent in the animal. A few hours later, when the guinea-pig was killed, only 1.6 mg. of histamine was found in the intestinal contents. The alimentary tract itself contained no histamine. In some way, 98.4 mg. of histamine had disappeared without causing death or eliciting any great symptoms. In another animal in which the same procedure was carried out, 4.7 mg. of histamine remained in the intestinal tract; 4.5 mg. had been transported to the liver. According to the authors, if the histamine that was not accounted for had been injected into the portal blood stream, the amount that would have entered the blood per minute would have been more than the dose necessary to kill a guinea-pig after a single intravenous injection. Results of the same nature were obtained when 500 mg. of histamine was administered orally to dogs.

Koessler and Hanke [9] also established comparisons between the minimum effective dose of histamine that would lower the blood pressure in the dog when injected into a systemic and into a mesenteric vein. They found the figure for a systemic vein to be 0.0027 mg. per minute per kilogram of body weight; 0.006 mg. was necessary to cause a decided reduction in the arterial pressure in a mesenteric vein. The increased capillary bed of the liver, Koessler and Hanke stated, is responsible for the increased amount of histamine necessary to effect a reduction in pressure on injection into a mesenteric vein. Dale and Laidlaw,[10] Meakins and Harington,[11] and Oehme [12] have made observations of the same nature with reference to intravenous injections of histamine into the portal and systemic circulations. This experiment demonstrates that the liver does not have a greatly detoxifying influence for histamine. Koessler and Hanke,[9] therefore, concluded that histamine is rendered pharmacologically inert in passing through the intestinal wall.

Just what the fate is of the histamine placed in the normal bowel or the bowel with severed gut obstruction is difficult to state. Some of it probably is absorbed but is detoxified in passing through the wall of the bowel. Koessler and Hanke's [6] failure to find histamine present in any quantity in the intestinal tract or its contents would indicate either that it

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9. Koessler, K. K., and Hanke, M. T.: Studies on Proteinogenous Amines; The Intestinal Absorption and Detoxication of Histamine in the Mammalian Organism, J. Biol. Chem. **59**:889, 1924.

10. Dale, H. H., and Laidlaw, P. P.: The Physiological Action of β Iminazolyl-ethylamine, J. Physiol. **41**:318, 1910-1911.

11. Meakins, J., and Harington, C. R.: The Relation of Histamine to Intestional Intoxication: II. The Absorption of Histamine from the Intestine, J. Pharmacol. & Exper. Therap. **20**:45, 1922.

12. Oehme: Ueber die Wirkungsweise des Histamins, Arch. f. expér. Path. u. Pharmak. **72**:76, 1913.

was almost completely absorbed and rendered innocuous in passing through the intestinal wall, or that it was destroyed within the lumen of the bowel. After histamine had been placed in a normal loop or segment of the bowel that had been obstructed previously, and a few cubic centimeters of the contents from such a loop had been aspirated and injected into a mesenteric vein, we were always able to elicit a decided histamine action after the lapse of an extended interval of time. The reduction in pressure accompanying such an injection was always greater and sustained for a longer time than the occasional reduction following the injection of intestinal contents from other segments in which histamine had not previously been placed. Gerard [5] stated that he was able to isolate 14 mg. of histamine from a closed colon loop in a dog eight months after Dragstedt had established the obstruction. In this animal either this amount of histamine remained in the bowel and resisted absorption as well as destruction in the lumen of the bowel, or it had its origin in the intestinal secretion formed by the mucosa of the obstructed segment. Koessler and Hanke [9] granted that their quantitative method for histamine determination in fecal content is only about 60 per cent effective.

Stone and Firor [13] intimated that in occlusion of the bowel, the distention per se, by increasing the intestinal pressure, is a big factor in absorption from the obstructed bowel. When histamine was placed in a segment of the intestine under a measured sustained pressure of 80 mg. of mercury, we were unable to detect any evidence of absorption of the histamine.

Meakins and Harington [11] placed histamine (histamine-phosphate) in various segments of the normal intestine in cats. They found that a rather sharp fall of pressure occurred a few seconds after the introduction was made. They stated this fall was more noticeable in the ileum, slightly less so in the duodenum and much less after the introduction of histamine into the stomach or cecum. When the blood pressure was gradually falling, they were unable to accelerate the fall by the introduction of more histamine. They believed that a sudden primary fall in pressure accompanying the introduction of histamine into the bowel should be the rule, and that failure to observe it may be due to the presence of semidigested food in the intestines.

We were never able to confirm this observation in the dog. Failure to depress the blood pressure even more on the introduction of a greater quantity of histamine into the bowel would indicate that no great amount of histamine as such was absorbed and would lend tenable support to

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13. Stone, H. B., and Firor, W. M.: Absorption in Intestinal Obstruction; Intra-Intestinal Pressure as a Factor, Proc. South. Surg. A. Abstr. J. A. M. A. 84:141 (Jan. 10) 1925.

the belief that the primary fall in pressure was not occasioned by histamine alone. Unless the blood pressure fell to such an extent that the animal was in a state of shock, the introduction of more histamine into the bowel, if absorbed as such, should depress the blood pressure as did the first injection.

It is generally known that ether anesthesia makes an animal much more susceptible[14] to the effects of histamine. It is stated that an unanesthetized dog can tolerate ten times the amount[15] that an animal under the influence of ether can. Most of our experiments on histamine absorption were made on etherized animals. Failure to elicit the histamine effect by placing it in the lumen of the bowel of these dogs with simple gut obstruction would indicate that no great amount of histamine was absorbed.

The marked fall in blood pressure that accompanies the release of the constricting mechanism in strangulation obstruction demonstrates that autolysis of the intestine deprived of its blood supply progresses rapidly and is accompanied by a rapid liberation of toxic material that gives a histamine-like effect. An effect of this nature was not observed when the kidney or splenic pedicle was clamped off for five hours. It was not seen after ligation of the aorta and vena cava for three hours. The accumulation of carbon dioxide behind the strangulation therefore was not the cause of the fall in pressure when the ligature was released. This fall in pressure seemed greater when there was venous stasis than in the presence of total anemia. This observation is in harmony with the statement of Bayliss[16] that the metabolism in the tissue is increased in the presence of venous stasis. Irrigation of the bowel at the time that the strangulation was established or just before the release of the obstructing mechanism did not prevent the fall in pressure when the ligature was removed. Tightening the ligature again usually brought about a rise of pressure, denoting that the absorption was disturbed. Replacing the removed intestinal contents in the bowel or injecting histamine into the lumen of the strangulated segment did not seem to accelerate the fall.

The only type of tissue in the wall of the bowel that differs materially from that of muscle, kidney or spleen is the mucosa. Depriving the intestine of blood probably occasions an autolysis of the mucosa of the bowel and therefore liberation of a toxic substance. It would seem

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14. Cannon, W. B.: Traumatic Shock, New York, D. Appleton & Co., 1923, p. 163. Dale, H. H.: Report of Shock Committee, Medical Research Committee No. 26, March 14, 1919, p. 15.

15. MacLeod, J. J. R.: Physiology and Biochemistry in Modern Medicine, St. Louis, C. V. Mosby Company, 1922, p. 308.

16. Baylis, W. M.: Principles of General Physiology, New York, Longmans & Company, 1924, p. 422.

that a damaged mucosa would be more permeable than the normal one to absorption from the lumen of the bowel. In these experiments, however, it would appear that autolysis of the wall of the bowel rather than an increased absorption from the lumen occasioned the depression of blood pressure.

Meakins and Harington [11] damaged the mucous membrane of the intestine by tying off the arterial supply of the part under investigation and then injected histamine. When the blood supply was arrested in this manner for from five to fifteen minutes and histamine was placed in the bowel, a marked primary fall was observed, but there was not a tendency toward a gradual and continued decline. This occurrence, the authors felt, indicated that the absorption of histamine took place rapidly and then almost ceased. Our observations would indicate that it was injury to the mucosa itself rather than absorption from the lumen that brought about the fall in pressure. We do not, of course, deny that absorption is not increased over that from the normal bowel or the segmentally obstructed bowel. As previously indicated this was our assumption, but the fall in pressure in the irrigated strangulated loop and the failure of the injected histamine to accelerate the drop in pressure would not support such a contention.

In the strangulations of short duration, only transient and slight reductions in blood pressure were observed when the constriction was released. In some instances, a fall in the pressure was not obtained. In the strangulations established a few hours previously, the fall in pressure was constant when the strangulation was released. In one animal (experiment 23, fig. 8), the blood pressure gradually declined, and the dog died as a result of this alone, although the pressure had been good before the constriction was released. In a few animals with strangulation obstruction, the pressure was low when the tracings were begun. In these animals it would appear that the visceral peritoneum of the strangulated intestine had become permeable to the toxic substance liberated by the damaged mucous membrane, and that absorption was occurring through the peritoneal cavity. For how otherwise could absorption occur with the lymphatics and mesenteric vessels obstructed?

It would also appear that when the blood supply to a segment of the bowel is disturbed by increasing the tension within the lumen a similar fall in pressure should be noted. Van Zwalenburg [17] has examined vessels of the intestinal wall with a cystoscope in the lumen of the bowel and has found that states of venous and arterial anemia may be produced by increasing the distention in the loop. The distention ulcer, however, observed so frequently on the antimesenteric border of the

17. Van Zwalenburg, C.: Strangulation Resulting from Distention of Hollow Viscera, Ann. Surg. **46**:780, 1907.

dog with an obstructed intestinal loop (both ends turned in) and in the patient with strangulation obstruction, is rarely seen in the patient with simple intestinal obstruction. We have never seen it in a large number of dogs in which simple obstruction of the gut has been established. The damage to the wall of the bowel in simple obstruction in which the intralumen tension is increased rarely approximates that observed in strangulation obstruction.

CONCLUSIONS

1. Absorption of histamine from the normal small intestine (duodenal and ileum, of the dog and in simple obstruction of the small intestine of two days' standing cannot be detected by the physiologic test for histamine.

2. In strangulation obstruction, a great fall in arterial blood pressure occurs following the release of the strangulating mechanism.

3. The autolysis of intestinal mucosa deprived of its blood supply is rapid and is accompanied by the liberation of a toxic substance that gives an effect like that of histamine.

4. The absorption of histamine from the lumen of a strangulated segment that is still viable does not appear to be great.

THIRTY-FIFTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY*

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CONGENITAL DEFORMITIES

Congenital Dislocation of Knee.—Spiers [1] reported four cases of congenital luxation of the knee. Of these, three were cases of double luxation and one of single luxation. In all cases the tibia and fibula were displaced forward, upward, and laterally. Only the patient with the single dislocation was treated by the author. Manipulative reduction was performed under an anesthetic and the deformity corrected, the knee being immobilized in plaster in a position of from 35 to 40 degrees flexion. Satisfactory progress was reported at the end of six weeks. when the patient was last observed.

Congenital Torticollis.—From a study of thirty-seven patients with wry neck observed at Spitzy's Clinic in Vienna during the last two years, Aberle [2] has drawn the following conclusions. Congenital wry neck is to be considered as "vitium primae formationis." It is found in association with other congenital deformities and may be present in several members of the same family. The patients may be classified in three groups: (1) patients with oblique posture of the head and asymmetry, but without discoverable changes in the sternomastoid muscle; (2) patients with marked changes in one of the sternomastoid muscles, but without evidence that the muscle was injured at birth, and (3) patients with injury of one of the sternomastoid muscles superimposed on a prenatal degeneration of the muscle. The author agrees that an

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* This Report of Progress is based on a review of 196 articles selected from 429 titles dealing with orthopedic surgery appearing in medical literature between July 2, 1927, and Sept. 24, 1927. Only those papers which seem to represent progress have been selected for note and comment.

1. Spiers, H. W.: J. Bone & Joint Surg. **9**:469 (July) 1927.

2. Aberle, W.: Ztschr. f. orthop. Chir. **49**:27, 1927.

injury to a normal sternomastoid muscle may be followed by the formation of an hematoma, but expressed the opinion that this heals in a short time and is not necessarily followed by wry neck. The asymmetry of the head and face associated with congenital wry neck is not hemiatrophy but the general reaction of the bone to pressure, with resulting hindrance of growth. The asymmetrical development tends to increase but may be arrested by early operative correction of the deformity.

[ED. NOTE.—Aberle's theory that injury of the sternomastoid muscle, sustained at birth, is not sufficient to account for congenital torticollis is interesting, but the evidence he has adduced is insufficient to prove his contention.]

Congenital Radio-Ulnar Synostosis.—Pepi [3] wrote on the subject of congenital radio-ulnar synostosis at the upper ends of the radius and ulna, and expressed the belief that the best method of restoring pronation and supination is the operation described by Galeazzi. This consists of a transverse osteotomy of the radius at a level a little above the insertion of the pronator radii teres, with the removal of a section of the bone, and the production of a pseudarthrosis at this point.

[ED. NOTE.—Authors who have made a study of congenital radio-ulnar synostosis have stated that excision of the head and neck of the radius usually fails to restore the rotary movements of the forearm. The synostosis usually recurs. Galeazzi's operation has advantages in this respect, as it is performed at a distance from the synostosis.]

ENDOCRINE DISORDERS AND THERAPY

Acromegaly.—In the annual oration delivered before the London Medical Society, Cushing [4] summarized the present knowledge of the function of the hypophysis. H. M. Evans is credited with the discovery that anterior lobe extracts would stimulate growth. It is difficult to obtain an active extract, and great variation is found in the commercial products. Experiments with the extracts have not produced acromegaly, but gigantism. Gigantism is probably the result of a process which has started before the epiphyses have become ossified, whereas acromegaly is an expression of the same influence acting after epiphysial growth has ceased. Cushing classified the pituitary syndromes as follows:

A. Apituitarism: Absolute privation of hypophysis probably leads through cachexia to death.

B. Hypopituitarism: 1. Anterior lobe deficiency due to ischemic necrosis (Simmond's disease). Simmonds reported thirteen cases of destruction, partial or complete, of the anterior lobe, many by septic infarcts. The counterpart of dwarfed animals thus exists in the dwarfed persons and results from disturbance of hypophysis in early life.

3. Pepi, C.: Policlinico **34**:205 (May 15) 1927.

4. Cushing, Harvey: Brit. M. J. **2**:1 (July 2) 1927.

2. Deficiency syndromes due to compression of parahypophyseal tumors (Fröhlich's disease). This syndrome is less cleancut than Simmond's disease, because of the different parts of the gland and of the adjacent structures that may be involved, particularly the hypothalamus. The patients are mentally alert, but show extreme degrees of adiposity or emaciation, polyuria or the reverse, dwarfism, sexual infantilism, or premature physical senility. Cushing has encountered in all, eighty-one verified examples of these parahypophyseal tumors. 3. Hypopituitary states associated with chromophobe adenomas. Of all pituitary syndromes these are most often encountered. Cushing had 188 in his series. They occur almost exclusively in adult life. The disorder is common, as common, in all probability, as goiter. One cannot diagnose this condition without definite local evidences of the growth. Changes almost always occur in adult life and are limited to the tendency to adiposity, loss of hair, sexual dystrophy, etc. It is not unusual for this condition to be treated as myxedema. Ordinarily the sella is greatly distended.

C. Dyspituitarism: This is a mixed group of syndromes in which hyperpituitary symptoms have been superseded by the reverse state.

D. Hyperpituitarism: 1. Gigantism.—Gigantism is due to chromophile adenomas originating in preadolescence. Cushing has seen sixty-five patients with such tumors. They are much oftener found in adults; hence acromegaly is much commoner. 2. Acromegaly—*acromophia* adenomas of adult life. Acromegaly calls attention to itself before the adenoma has reached the tumefaction stage. Cushing feels justified, in view of the low mortality (41 per cent), in attacking the tumors early while the sella was still small. He noted as postoperative results: (1) loss in weight; (2) lowered metabolic rate, and (3) relative intolerance to carbohydrates. By partial hypophysectomy the intolerance may be reduced and existent glycosuria checked. Complete extirpation is to be avoided lest diabetes insipidus, excessive adiposity, and even a fatal cachexia supervene. Only when substitution therapy has been made practical will this risk be overcome.

Davidoff and Cushing [5] stated their belief that acromegaly represents a state of hyperpituitarism of the acidophil cells of the pars anterior. They consider that there are ample reasons in support of the view that the meliturias which occur in 25 per cent of all cases of acromegaly are primarily hypophyseal, even though the pancreatic islets play a secondary rôle in their production.

In seven patients with acromegaly (four women and three men), Castex and Schteingart [6] found the basal metabolism increased in three

5. Davidoff, L. M., and Cushing, Harvey: Studies in Acromegaly, Arch. Int. Med. **39**:751 (June) 1927.

6. Castex, M. R., and Schteingart, M.: Rev. Soc. de med. int. y tisiol **3**:66, 1927.

and normal in four. The largest increase was 31 per cent. They concluded from their studies that simple acromegaly without change in the tubers or in the posterior lobe of the pituitary causes an increase in metabolism. The complicated type of acromegaly does not produce this effect.

Parathyroid Hormone and Calcification of Fracture Callus.—Lehman and Cole [7] conducted some experiments on animals to determine the effect of injections of parathyroid extract on the calcification of fracture callus. *A priori* they did not believe that the extract would hasten or aid in inducing the deposit of callus, because its action is to mobilize the fixed calcium in the body, and as Hunter and Aub have shown, the excess of calcium in the blood serum of patients who have had parathyroid extract comes largely from the bones. The results of the experiments show that parathyroid extract does not hasten the calcification of fracture callus. The only effect noted in rats is a tendency to delay the process.

On the other hand, Hueper [8] performed some experiments which led him to draw the opposite conclusion. He stated that repeated injections of parathyroid extract apparently stimulate the production and calcification of osteal tissue. However, the extract cannot be used without danger, as evidenced by the finding of areas of necrosis in the myocardium and the cortex of the suprarenal gland in animals which have received repeated injections of it.

[ED. NOTE.—The work of Hunter and Aub clearly demonstrates that continued administration of parathyroid extract causes increased elimination of calcium from the body and in time leads to decalcification of the bones.]

DEVELOPMENTAL DISEASES

Osteochondritis Ischiopubica.—Attention has been called by Wuelfing [9] to a condition which he has named osteochondritis ischiopubica. The clinical picture resembles that of hip disease, although the symptoms are less severe. The condition consists of a disturbance of the ossification of the cartilage at the point of junction of the ischium and pubis in the acetabulum. An appearance of haziness and globular thickening develops. According to the author, the condition should be suspected when a patient complains of an indistinct disturbance of the gait, though on roentgen-ray examination the femoral head and the hip joint appear normal.

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7. Lehman, E. P., and Cole, W. H.: Parathyroid Hormone and Calcification of Fracture Callus, J. A. M. A. **89**:587 (Aug. 30) 1927.

8. Hueper, W.: Effect of Repeated Injections of Parathyroid Extraction on Calcification of Osteoid Tissues, Arch. Path. **3**:1002 (June) 1927.

9. Wuelfing, M.: Deutsche Ztschr. f. Chir. **199**:413, 1926.

Osgood-Schlatter's Disease in Adults.—Opposing the opinion of other authors, Brandes [10] stated that Osgood-Schlatter's disease of the tibial tubercle occurs not only in young growing persons, but also in adults. He cited as an example the case of a man, aged 48, who showed the characteristic clinical signs and typical roentgenologic appearance. The symptoms dated from a strain received during the war. The examination showed that the apophyseal lines of the tibial tubercles of both knees had failed to ossify during the years of growth and had persisted as points of reduced resistance to strain. Brandes stated that he has seen a number of examples of the same condition in young adults of about 20 years. In the patients with only mild symptoms he usually found conservative treatment sufficient, but when the condition was persistent he employed operative treatment. The operation consisted in splitting the patellar tendon, exposing the tubercle, and removing the affected area with the curet.

[ED. NOTE.—While symptoms may not arise until adult life, we do not believe that Brandes meant to infer that the condition originates then. The main fact is that Osgood-Schlatter's disease may go on in youth to complete failure of union between the apophysis of the tubercle and the tibia, and that the fibrous connection may yield to strain in later years. One of us has encountered this condition in young adults, and at operation found the tubercle entirely loose. Removal relieved the symptoms.]

Vertebral Epiphysitis.—Zur Verth [11] has encountered in children a developmental disease of the spine that evidently corresponds to what other authors have described as vertebral osteochondritis. He found the condition limited to a single vertebra. In the early stage there is an appearance of marked atrophy of the vertebral body, with an irregular zone in the middle. In the later stage the body appears to diminish to a narrow plate which represents the central dense zone, while the adjacent areas disappear. The symptoms may resemble those of Pott's disease, but the author felt that he could exclude the possibility of tuberculosis, typhoid fever, syphilis, or trauma. He considers the condition to be related to Koehler's disease of the scaphoid and to other similar diseases, and proposes the name "vertebra plana."

Clinical Importance of the Os Tibiale Externum or Accessory Tarsal Scaphoid.—Calling attention to the clinical importance of the os tibiale externum or accessory scaphoid, Sever [12] stated that this condition may be of medicolegal significance, especially following trauma, because of the possibility of its being mistaken for a fracture. It is generally associated with badly pronated and relaxed feet which are particularly

10. Brandes, M.: München. med. Wchnschr. **74**:1830, 1927.

11. Zur Verth: Ztschr. f. orthop. Chir. **48**:70, 1927.

12. Sever, J. W.: Clinical Importance of Os Tibiale Externum or Accessory Tarsal Scaphoid, J. A. M. A. **89**:359 (July 30) 1927.

resistant to corrective treatment. He has reached the point of view that in such cases when the feet are persistently painful, operative treatment is necessary. The operation consists of an arthrodesis of the astragaloscaphoid joint, with removal of the accessory scaphoid and shortening of the tendon of the tibialis posterior muscle.

NUTRITIONAL DISEASES

The chemical changes found in rickets have been discussed by Gamble,[13] who pointed out that the disease depends on a reduction, not only of the calcium in the blood plasma, but also of phosphorus. Since the calcium content is nearly stationary in ordinary rickets, the measurement of the phosphorus content of the blood plasma gives the degree of rickets. In tetany the blood calcium is materially lowered. The dietary studies have shown that an unknown substance "D" is necessary to keep the calcium and phosphorus balance up to normal. The same effect is produced by sunlight. This substance "D" is present in abundance in cod liver oil. He pointed out that from a practical point of view the important result of the recent studies of rickets has been the rediscovery of the curative action of cod liver oil and sunlight.

Hess [14] found that cholesterol when irradiated with ultraviolet light possesses antirachitic properties, and that bran, which contains a large amount of this substance, may be used successfully. Ergosterol prepared from yeast is the only sterol found which acquires antirachitic activity on exposure. He stated that irradiated yeast may be used, and also irradiated dried milk, the milk being the most successful.

Renal Rickets.—Smith and Walsh [15] studied the case of a patient with renal rickets and reviewed the literature on this subject. The clinical picture in their own case corresponded identically with that of the other reported cases, and at autopsy chronic nephritis was found. The symptoms in all cases have been strikingly similar. The onset is insidious and the development is not markedly retarded until the sixth or seventh year. As the children grow older, the retardation of growth becomes more and more marked, and bony deformities develop. Genu valgum, the most characteristic and frequently found deformity, is usually observed about puberty. Polydipsia and polyuria are usually present. The specific gravity of the urine varies from 1.004 to 1.008. Albuminuria is present in all cases, and at times a few hyaline casts are seen. Roentgenologic examination reveals multiple fractures and general osteoporosis. In a number of the reported cases diagnosis was made at autopsy, death having been caused by uremia following orthopedic operations.

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13. Gamble, J. L.: Boston M. & S. J. **197**:373 (Sept. 8) 1927.

14. Hess, A. F.: Antirachitic Activity of Irradiated Cholesterol, Ergosterol and Allied Substances, J. A. M. A. **89**:337 (July 30) 1927.

15. Smith, D. C. W., and Walsh, M. D.: South. M. J. **20**:437 (June) 1927.

Brockman [16] also reported his observations on three patients with the same condition. There was the same association of late developing bone deformities with chronic nephritis. He was able to obtain at autopsy a tibia and fibula from one of the patients for pathologic examination. The chief descriptive points obtained from this study are as follows: 1. The shafts of the bones in renal rickets are straight, and the deformities are due to separation and displacement of the epiphyses. (It is not desirable to correct the deformities because of the danger of uremia and the tendency to recurrence.) 2. The red marrow is replaced by fat marrow. 3. There is little bone formation. 4. Active bone absorption by osteoclasts takes place in the neighborhood of the growth disks and also of the shaft. 5. The absorbed bone is replaced by fibrous tissue. 6. The walls of the arteries in the medulla are thickened. 7. An increase in the number of capillaries is observed in the region of the growth disk.

Osteitis Deformans.—Van Hazet and Andrews [17] made a study of osteitis deformans, or Paget's disease, with careful chemical and laboratory examinations of a group of patients. They recited briefly the history of the disease and the various theories concerning its etiology. Their own studies yielded the following results: 1. Chemical analysis of the blood and excreta showed that there was calcium retention despite a fall in the blood calcium. 2. An unusually rapid rise in the rate of absorption of sugar was noted. 3. The administration of epinephrine hydrochloride caused a decrease in the blood calcium. There was also a quick response of the blood pressure and a rapid return to normal. From this fact they concluded that in Paget's disease there is a polyglandular disturbance of internal secretion resembling parathyroid disturbance. They explained the pathologic picture as an increase in the permeability of the tissues entailing an inability of the osseous structure to retain calcium and the entire condition as due to a hypersecretion of the parathyroid gland.

ANATOMIC STUDIES

Symmetry of the Bones in Fetal Life.—Koenig and Kornfeld [18] examined and measured the length of the bones in forty-two embryos and infants, and found that asymmetrical development of the bones, especially in respect to length, is common in fetal life, but generally disappears before or shortly after birth. The left clavicle and the left scapula are generally longer than the right clavicle and right scapula. The upper ribs on the left side also are usually longer. The relations between the length of the long bones of one extremity and of the bones of the leg to the bones of the arm change constantly during fetal life.

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16. Brockman, E. P.: Brit. J. Surg. **14**:634 (April) 1927.

17. Van Hazet, Willard, and Andrews, Edmund: Surg. Gynec. Obst. **45**:54 (July) 1927.

18. Koenig, K., and Kornfeld, W.: Ztschr. f. d. ges. Anat. **82**:657, 1927.

Mechanics of the Patella.—An investigation of the mechanics of the patella was reported by Moloney.[19] He reached the following conclusions: The patella is not a lever, and the femoral condyles do not constitute an efficient inclined plane. The patella owes its efficiency to the fact that it increases the distance between the axis of rotation of the tibia and the line of direction of the force that pulls on the tibial tubercle by means of the patellar ligament.

Metatarsus Atavicus.—Under the term "metatarsus atavicus" Morton [20] described the condition in which the first metatarsal bone is shorter than the second. The symptoms simulate those of other metatarsal disorders. The diagnosis depends on the roentgenologic examination.

CHRONIC ARTHRITIS

Sulphur Metabolism.—Cawadias [21] made a study of the sulphur balance in persons with arthritis deformans, employing a method originated by himself. The study included observations on thiopexy (that special metabolic function of the organism through which the sulphur equilibrium is maintained), sulphur oxidation, and sulphur conjugation. He found a deficient thiopexy and increase in sulphur catabolism. Sulphur oxidation was not disturbed and sulphur conjugation, in some cases, was increased. He concluded that colloidal sulphur treatment may be of use in certain patients with arthritis.

Gastric Function.—Miller and Smith [22] made an investigation of gastric function by means of the test meal in a group of 250 patients with different types of chronic arthritis. They found that the incidence of achlorhydria and hypochlorhydria in chronic arthritis was five times as great in their group of patients as in normal subjects. Streptococci were isolated in 92 per cent of fecal cultures. Both observations, while abnormal, do not differ from those encountered in a wide variety of other diseases, and, therefore, the authors concluded that these are not primary etiologic factors, but that achlorhydria may allow more ready multiplication of bacteria in the bowel and may be an accessory factor.

Basal Metabolism.—A careful study of the basal metabolism in 200 patients with chronic arthritis was made by Swaim and Spear.[23] The patients were divided according to the classification of Goldthwait, Painter, and Osgood. They found that age, duration of disease, and activity of the disease do not have any effect on the metabolic rate. In the atrophic and hypertrophic types the tendency has been toward a minus rate. In some of the patients, treatment by thyroid extract was attended by an immediate further drop in the metabolic rate. As the

19. Moloney, J. C.: J. Bone & Joint Surg. **9**:476 (July) 1927.
20. Morton, D. J.: J. Bone & Joint Surg. **9**:531 (July) 1927.
21. Cawadias, A. P.: Lancet **1**:1283 (June 18) 1927.
22. Miller, S., and Smith, F. B.: Quart. J. Med. **20**:271 (April) 1927.
23. Swaim, L. T., and Spear, L. M.: Boston M. & S. J. **197**:350 (Sept. 1) 1927.

dose of thyroid extract was increased, a return to the normal rate and a more stable metabolism was noted. This was accompanied by an amelioration of the symptoms.

Juvenile Rheumatism.—From a statistical study of the incidence of rheumatic fever in children in London, Benjamin [24] concluded that it is a disease of poor people and that the incidence of the disease is in direct relation to the degree of the poverty.

Miller [25] made a comparison between the reports of the British Medical Association and those of the Medical Research Council on arthritis, and drew the following conclusions in regard to the importance of six supposed etiologic factors: 1. Influence of social status. They agreed that it is a disease of the poor, but not necessarily of the poorest. 2. The influence of heredity. It was agreed that heredity is of no influence. 3. The influence of school environment. The home rather than the school is the causative factor, as those children who were taken from homes in the "rheumatic stratum" and placed in special schools escaped. 4. The influence of tonsillar disease and tonsillectomy. Diseased throats were found in from 75 to 83 per cent of the patients. The removal of the tonsils does not prevent chorea. 5. The influence of contagion. Contagion is, at most, of the slightest importance. 6. The influence of damp dwellings. "There is nothing in the theory of damp houses as a causative factor."

Incidence of Hypertrophic Arthritis.—Garvin [26] made an investigation of the incidence of hypertrophic arthritis of the spine in a series of 2,090 patients more than 50 years of age, who, without complaint of symptoms in the back but because of suspected urinary disorders, were subjected to roentgenologic examination of the kidneys, bladder and ureters during 1925. What Garvin designated as "incidental hypertrophic arthritis of the spine" was found in 40 per cent of the women and in 67 per cent of the men. Garvin discussed the possible etiologic factors, such as abscessed teeth, infected tonsils, etc., the presence of a traumatic factor, such as obesity, in which the assumption of chronic trauma can be made and also the evidences of senescence. He stated that in view of the high incidence in persons beyond 50 years of age, especially in men, of hypertrophic arthritis of the spine, unaccompanied by any symptoms in the majority of the patients, the condition should be considered and treated conservatively. He pointed out the obvious improbability of any single accident or injury being responsible for the development of hypertrophic arthritis.

Hypertrophic Arthritis of the Cervical Spine.—Forrestier [27] described various thickenings noted on the transverse processes of the cervical

24. Benjamin, F. J.: Lancet **1**:1175 (June 4) 1927.
25. Miller, Reginald: Brit. M. J. **1**:952 (May 28) 1927.
26. Garvin, J. D.: Hypertrophic Arthritis of Spine, Arch. Surg. **15**:118 (July) 1927.
27. Forrestier, Henri: Lancet **2**:65 (July 9) 1927.

vertebrae in patients suffering from chronic arthritis. He expressed the opinion that these thickenings frequently give rise to occipital headaches and neuralgic pains radiating down the arms.

That osteo-arthritis of the cervical spine may cause serious pressure on the nerve roots, was pointed out by Hendry and Fowler.[28] They examined a patient who showed marked muscular weakness and sensory disturbance of one arm, without pain, in whom the symptoms were ascribable only to this cause.

TUBERCULOSIS

Remote Results of Operative and Nonoperative Treatment for Tuberculosis of the Ankle in Children.—Pouzet [29] made an investigation of the results of treatment, both nonoperative and operative, in children with tuberculosis of the tibiotarsal articulation in Nové-Josserand's clinic at Lyon. The statistics cover a group of 104 patients, all children under the age of 16, who were treated between 1898 and 1922, inclusive. The minimum period of observation was three years. The study was limited to those cases in which the primary focus of disease had been in the tibio-astragalar articulation, with or without secondary invasion of other bones or joints, and did not include those with diffuse lesions starting simultaneously in all the tarsal bones. It has been the general policy in the clinic to employ immobilization as the best method of treatment, except in rare cases in which the severity of the process or the presence of a complication made surgical intervention necessary. The parts were encased in plaster, and the casings changed at intervals of three months. Open air, sunlight, and other antituberculous measures were also employed. When the tuberculous process appeared to extend, or when progress seemed to be uncertain, surgical intervention was resorted to. The results were graded as: normal—meaning absence of functional impairment; very good—excellent function, but with minor troubles, such as limp when tired; good—slight limp, with walking capacity exceeding 10 kilometers; fairly good—limp, with walking capacity of from 5 to 10 kilometers; and bad.

The results in general in a total of 104 patients, of whom ninety-one were treated by immobilization, were as follows:

Cure was obtained in sixty cases, or 66 per cent; in eighteen the feet were normal; in twenty-eight the results were very good, and in fourteen the results were good or fairly good. (Four of these patients died later, after the local lesions had healed.)

Failure resulted in thirty-one cases, or 34 per cent. Four patients died during treatment; twenty-seven required operative intervention, twenty because of extension and seven because of recurrence.

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28. Hendry, A. W., and Fowler, Andrew: Lancet **1**:1181 (June 4) 1927.
29. Pouzet, F.: Rev. d'orthop. **14**:99, 1927.

Just as good results were obtained in the cases in which sinuses were present as in those in which they were not. The younger the patients the better were the results. The severity of the disease seemed to increase with age, and the older the patients the higher the number of deaths and the greater the necessity for resorting to operative treatment. The cures were fairly permanent, with recurrence in only 3.5 per cent of the patients. The author does not consider ankylosis the best result, but, on the contrary, stated that a certain degree of mobility helps in walking, without apparently increasing the risk of recurrence. Roentgen-ray examination showed a perfectly normal foot in a few cases; in others, lesions limited to the articular surfaces, such as irregularity of the joint space, exostoses and osteophytes, fibrous and bony ankylosis, and flattening of the astragalus. Hypermobility developed in the uninvolved joints to compensate for stiffness in the diseased joints. The diseased foot showed retardation of growth, and was always shorter than the normal one. In a few cases there was a shortening of the tibia of from 1 to 3 cm. No deformities of the foot were noted except pes cavus in three instances.

The patients in whom conservative treatment failed (thirty-nine of 104) and operative measures had to be employed also were studied. The cases were classified as follows: twenty-five late interventions after immobilization was tried, eighteen because of aggravation, and seven because of early recurrence; fourteen early interventions necessitated by the extent and severity of the process. The operations consisted in astragalectomy and localized tarsectomy. In the beginning, the proportion of astragalectomies was high, but as the efficacy of more conservative procedures was demonstrated, the number of astragalectomies decreased. Bony lesions were noted in the astragalus thirty-nine times, in the tibia twenty, in the calcaneum twenty-five, in the scaphoid two, and in the cuboid five. The average period required for a cure with complete healing of sinuses and the possibility of walking was about eleven months after astragalectomy and thirteen months after tarsectomy. Of the thirty-nine patients, cures were obtained in twenty-eight, or 73 per cent; on one amputation was performed, and one is still under treatment. There were nine deaths, or 23 per cent. The fatalities occurred chiefly in young patients and were due to the severity of the process rather than the result of the interventions. From a study of the results the author concluded that operative treatment is capable of preserving a useful foot in a large number of patients with tuberculosis of the posterior tarsus. Although the results of the two methods cannot be compared because of the difference between the disease processes in the two groups, Pouzet stated his belief that treatment by immobilization should be tried in children, and that only after a thorough trial without improvement, or in the case of a severe lesion, should surgical intervention be employed.

[ED. NOTE.—We wish to call attention to the fact that when patients with supposed tuberculosis of the joints are treated nonoperatively, it is always difficult to be certain of the diagnosis.]

POLIOMYELITIS

In a recent editorial in the *Journal of the American Medical Association,*[30] the knowledge of infantile paralysis has been well summarized. Cases of poliomyelitis have been divided into three classes: (1) those with characteristic paralysis; (2) those without paralysis, but exhibiting symptoms indicative of meningeal irritation and usually minor disturbances of the motor centers, the so-called abortive type, and (3) those showing symptoms similar to the initial symptoms of known cases of infantile paralysis, but without definite indications of involvement of the central nervous system. In discussing the treatment it has been stated that there is every reason to believe that rough handling of the spine and manipulation, as practiced by chiropractors and members of other cults, renders impossible the recovery which might otherwise take place in some of the affected nerves. The author considers that the only effective method of prevention is complete isolation from contact with patients in all stages of the disease, including convalescents and carriers. It has been recommended that during an epidemic until cold weather sets in children should not travel about any more than is absolutely necessary. No specific prophylactic treatment that can be applied practically has yet been discovered.

We have noted a recent report by the Council on Pharmacy and Chemistry of the American Medical Association[31] of its refusal to accept for inclusion in New and Nonofficial Remedies poliomyelitis antistreptococcus serum. This action was based on the following objections: 1. The organism from which the serum is produced is not generally accepted as the etiologic agent of poliomyelitis. 2. The published reports on the serum are generally favorable, but there is considerable question as to whether the groups of control cases are directly comparable. 3. It has been found that on account of widespread favorable newspaper publicity given the serum, the physician often feels compelled to use it, though he is not convinced of its efficacy. Indeed, laymen often demand its employment. In our estimation, the Council has taken the proper stand in refusing to accept any poliomyelitis antistreptococcus serum until more positive evidence for its usefulness becomes available.

PYOGENIC INFECTIONS

Osteomyelitis.—In discussing infections of the bones and joints in children, Stone[32] pointed out that while epiphyseal separation is well

30. Infantile Paralysis, Editorial, J. A. M. A. **89**:1062 (Sept. 24) 1927.

31. Poliomyelitis Antistreptococcus Serum, Reports of Council on Pharmacy and Chemistry, J. A. M. A. **90**:617 (Feb. 25) 1928.

32. Stone, J. S.: Boston M. & S. J. **197**:507 (Sept. 29) 1927.

recognized, the frequency with which an epiphysis may be loosened without actually being displaced is not generally appreciated. Similarly, subperiosteal and greenstick fractures are seen more often in children because of the relatively greater thickness of the periosteum. The importance of these and other mild injuries in relation to infection lies, according to the author, in the fact that areas of increased susceptibility to infection are produced in the regions of the epiphyses by the trauma.

Bocchini [33] also has been convinced from a study of the literature that trauma plays an important part in providing an area of lowered resistance in the bone to infection. Discussing acute osteomyelitis of the spine, he stated that the vertebral body is involved more commonly than the neural arch. If the body is involved the prognosis is grave; if the neural arch is involved it is less grave. Of the neural arch the author has found the lamina more often affected, but either the spinous process or the transverse process may be affected. When the involved area of the spine is accessible he has recommended surgical intervention.

Control of Wound Infection.—Orr [34] pointed out the necessity of following three fundamental rules in the treatment of infected wounds: (1) a thorough primary operation, aseptically performed; (2) the avoidance of secondary infection in the postoperative dressings, and (3) immobilization, in correct position, of all injured parts until healing has been established. He advocated packing the wounds with gauze on which petrolatum has been smeared, and fixation of the parts in plaster at the time of operation. By this method he considers it unnecessary to change the dressings more often than at intervals of from three to four weeks, and not infrequently the infected bone cavities heal completely with only one or two dressings.

[ED. NOTE.—Approaching this method with grave doubts as to its safety and recognizing its possible dangers unless the patients are carefully watched, we have been able to confirm Orr's claims in a small group of cases. We agree that the thoroughness of the operation is of prime importance and that unnecessary postoperative dressings are to be avoided. Whatever other arguments may be advanced in support of this method, the humanitarian one of reducing painful dressings to a minimum, especially in children, is a powerful one.]

VASCULAR DISEASES

Thrombo-Angiitis Obliterans.—Lian, Puech and Viau [35] made an investigation of fifty-two patients with endarteritis obliterans, with the purpose of shedding some light on the etiology of the disease. Dis-

33. Bocchini, A.: Pediatria **35**:554 (May 15) 1927.

34. Orr, H. W.: Minnesota Med. **10**:362 (June) 1927.

35. Lian, Puech and Viau: Bull. et mém. Soc. méd. d. hôp. de Paris **51**:534 (May 5) 1927.

cussing probable causes, they stated that acute or chronic infection or acute-intoxication, as in diabetes or gout, may be factors in rare cases. Nutritional diseases occurring about the age of 50 probably play an important part. Tobacco occupies a considerable rôle, while that of syphilis is insignificant. The writers do not regard Buerger's disease as a pathologic entity, but merely as a clinical form of endarteritis obliterans occurring with greatest frequency among the Jews of Central Europe.

Guillaume [36] has made a study of the pathologic lesions in Buerger's disease, employing serial sections covering the entire length of the diseased arteries. As a result of his examinations he does not agree with Buerger's views, namely, that thrombosis constitutes the primary feature of the disease, with secondary parietal changes affecting the vessel walls. Guillaume expressed the opinion that the primary lesion is a proliferating endarteritis which obliterates the lumen of the vessel and leads to thrombosis in the blind culdesac of the artery above that point.

The Operation of Embolectomy in Embolic Disturbances of the Extremities.—Key [37] has performed the operation of embolectomy on ninety-five patients and is convinced of its value. In discussing his experience, he stated that the embolus is usually found at the point of division of an artery, and that if it does not at first completely occlude the vessel it quickly grows (from a few hours to several days) until it shuts off the blood supply entirely. To determine the seat of the embolus is difficult. Usually it is considerably higher than the region of circulatory disturbance. Palpation of the arterial pulsation may indicate the point of lodgment, but often the pulse is weak as a result of the weak heart. The diagnosis is easy when the embolus causes primary occlusion of the artery, but when the occlusion is only partial, it is much more difficult. Key found great advantage in local anesthesia, and advises that the operation be performed with this aid. He followed the technic of Carrell, using fine needles and sutures of silk sterilized in petrolatum. Gauze moistened with a 2 per cent solution of sodium citrate is used, and the instruments and gloves are rinsed in the same solution. The artery, after being compressed with a soft clamp, is opened somewhat above the point of suspected lodgment of the embolus. By careful traction even long emboli may be removed, but sometimes it is necessary to make a second opening in the vessel. When the embolus does not slip out easily, one must try to strip or massage it upward from below. The prognosis depends on the time elapsed between the lodgment of the embolus and its removal, the situation of the embolus, and the general condition of the patient, especially the heart.

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36. Guillaume, A. C.: Bull. et mém. Soc. méd. d. hôp. de Paris **51**:611 (May 12) 1927.

37. Key, Einar: Zentralbl. f. Chir. **54**:2190 (Aug. 27) 1927.

NERVE DISTURBANCES

Treatment of Spastic Paraplegia by Sympathetic Ramisection.—Royle [38] reaffirmed his original opinion of the value of ramisection and described the late results of the operations he performed some years ago. Defending his experimental work, he wrote that "although a number of investigators have failed to verify my results, no one has attempted to reproduce them on the goat, the animal which I used." In the article, he repeated the story of his first operation on a patient, Sept. 1, 1923. The improvement in this patient persists to date, three years after operation. Besides changes in tone, he enumerated the following results: increased temperature, improvement in muscular control, improvement in balance, disappearance of tremor, and increase in the size and strength of the limb. Coming to the subject of congenital spastic paraplegia, he noted two main types: (1) the rigid type and (2) the choreic type. In the first group he distinguished (*a*) cases in which the patient retained or had developed muscular control; (*b*) cases in which voluntary control was not present. He performed ramisection in twenty-six patients with spastic paraplegia of both lower limbs. All were of the rigid type except one of the choreic type. He analyzed his results as follows. Walking: There was diminution in disability in all but one patient. Before operation sixteen of twenty-six could not walk alone. Fourteen of these patients learned to walk within six months after operation. Changes in Tone: Rigidity invariably diminished and a wider range of movement developed. Balance: Increased facility in balance was an invariable postoperative result. Performance of Active Movements: "Almost every patient reported increased facility in performing active movements." Speed: Speed was always increased. Inhibition: Improved inhibition was a consistent result when the tone was great enough to impede normal movement. Changes in Condition of the Viscera: Seventeen of the patients were suffering from chronic constipation. Thirteen of this number "were more or less relieved." Vasomotor Changes: Every patient in the series exhibited postoperative vasomotor changes. The acute changes were transitory, but a definite increase in temperature and freedom from vasomotor disorder persisted after ramisection. In respect to structural changes such as contractures, the author stated that these must be dealt with surgically before the full effect of ramisection is apparent. In one patient who showed choreiform movements, improvement in function was definite and there was a lessening of the movements.

38. Royle, N. D.: M. J. Australia **1**:632 (April 30) 1927.

(To be continued)

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